Archives of Dermatology and Syphilology

VOLUME 42 DECEMBER 1940 NUMBER 6

COPYRIGHT, 1940, BY THE AMERICAN MEDICAL ASSOCIATION

OCCUPATIONAL LEUKODERMA

EDWARD A. OLIVER, M.D.
CHICAGO
AND
LOUIS SCHWARTZ, M.D.
AND
LEON H. WARREN, M.D.
WASHINGTON, D. C.

In May 1939 an insurance company requested the examination of a group of men employed in a tannery near Chicago. These men had instituted suit against the tannery, claiming that a peculiar depigmentation of the skin, which had developed on their forearms and hands, was the result of wearing a certain type of rubber glove. A visit was made immediately to the tannery, and on the first day 20 of these men were examined. All of them showed this unusual type of depigmentation, some more than others. Thirteen of them were Negroes, 3 were Mexicans and 4 were white. In 7 of the Negroes and in 2 of the Mexicans the depigmentation was especially evident, extending over the backs of the hands and up the forearms, ending in an abrupt line halfway up the forearms. The involved areas corresponded with those covered by a heavy rubber gauntlet type of glove they had been wearing (fig. 1). In these cases the areas of leukoderma were milky white, in striking contrast to the dark skin of the Negroes. The contrast was not so great in the lighter-skinned Mexicans and was much less in the white men. Even in the most pronounced cases the palms and the dorsal aspects of the terminal phalanges of the fingers were unaffected.

In 6 of the other Negroes the depigmentation was irregular, occurring in streaks and spots, and in 1 of these there were only definite rims about ¾ inch (1.9 cm.) in width on the forearms where the upper ends of the gloves touched (fig. 2). When questioned about this he stated that after he had worn his gloves several months he had experienced some itching and irritation of the skin in these areas and had never worn them again.

Read at the Sixty-Third Meeting of the American Dermatological Association, Inc., Colorado Springs, Colo., June 1, 1940.

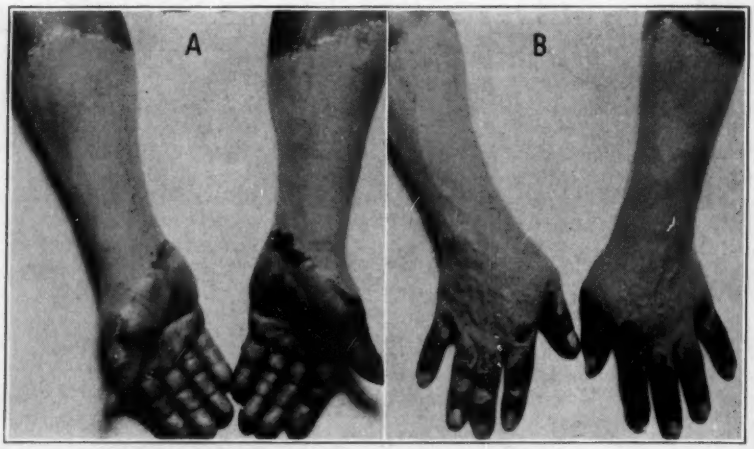


Fig. 1.—Leukoderma of the forearms showing (*A*) absence of involvement of the palms and (*B*) absence of involvement of the dorsal aspect of the fingers.

Fig. 2.—Rims on the forearms at the upper margin of the gloves in a patient who discarded the gloves after wearing them for a short time.

Three of the Negroes showed patches of depigmentation in the region of the biceps, the result of flexing their gloved arms against the biceps. One patient had several small patches on the right side of his face, the result of wiping perspiration away from his glasses. One man showed striking depigmentation (fig. 3) on the abdomen, upper part of the thighs and buttocks. This could not be explained except that it was possibly due to rubbing sweat and water off his body.

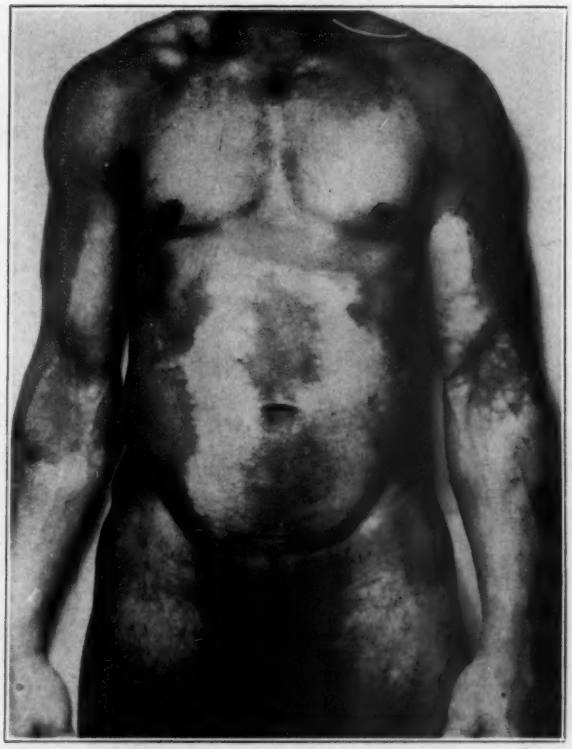


Fig. 3.—Involvement of the abdomen, thighs and chest, in addition to the involvement of the forearms.

The skin of none of these men showed signs of acute or chronic dermatitis in any of the leukodermic areas. In some cases the hair had disappeared, and in others it was short and stubby as if it had once been removed and had grown back. In a few instances it was unaffected. None of the hairs were depigmented. As these men were constantly in contact with chemicals used in the tanning of leather, it was felt that these chemicals could have been responsible for the depilation. An additional interesting feature was the behavior of the hair follicles. The

pigment about them seemed the last to disappear and the first to reappear (fig. 4).

These men were intelligent and answered questions readily. Some said their leukoderma had been preceded by itching and the development of a mild dermatitis; others said they had not noted any irritation or itching. All of them stated the belief that the rubber gloves were the cause of their troubles, but as they were constantly in contact with

Fig. 4.—Absence of follicular involvement; pigmentation still remains about the follicles.

irritating chemicals, it was our opinion that the problem required careful study.

The office of the Dermatoses Investigations of the United States Public Health Service had received a report of these cases and had already been approached by the Department of Leather Research, by the representatives of the rubber company who manufactured these gloves and also by another tannery at which the employees had a similar type of depigmentation.

An investigation was begun immediately in tannery 1. Only 48 employees out of a total of 88 employed in four departments wore the rubber gloves. Of the 48 who wore the gloves, 25 (52 per cent) had leukoderma. Ten men of 11 employed in the tan house wore gloves, but only 6 had leukoderma, a percentage of 60. Of 4 workers in the hand finishing department, only 2 wore gloves, and both of them were affected. Thirteen of 16 employed in the color and fat liquor departments wore gloves, and 7 of these had leukoderma, a percentage of 54. Only 22 of 57 employees of the beam house wore gloves, but only 9 of them had leukoderma, a percentage of 41. The janitor who cleaned the plant also wore gloves and had leukoderma.

In commenting on the presence of leukoderma in some and its absence in others engaged in the same type of work, a foreman expressed the belief that time was a considerable factor. The men worked for odd periods of time, and he had noted that those who wore the gloves the longest were the most severely affected. Personal susceptibility undoubtedly was also a factor.

Because of this we felt that possibly the p_H of the skin might vary in some of them and be a contributing factor. Eleven of the affected men and 11 unaffected were tested. The location of the test was the chest in 6 cases and the forehead in 5. The p_H of the skin of all but 1 of the affected men was 5.0 to 5.7; in 1 case the p_H was 5.9 to 6.1. Three of the men most severely affected perspired little as compared with the others. In 11 unaffected workers, 4 of whom did not wear gloves, the p_H was 5.9 with 2 exceptions; in 1 it was 4.7 and in the other 5.0. From these tests it would seem that the p_H of the skin played no part as an etiologic factor.

The employees had made so many complaints to the management about a curved finger glove, no. 62, which they had been wearing since April 1937 that they discontinued using it, thinking it was the cause of the trouble. A straight finger glove, no. 6, which had always been used up to April 1937, was substituted, and the men were apparently satisfied that they had removed the source of their leukoderma.

When we looked about for further clues, it was learned that dimethylamine was used as an unhairing agent. Since this chemical is not commonly used in tanneries, it was suspected that it might have been an etiologic factor, but this idea was abandoned when a second tannery was visited. The same type of leukoderma had developed here, but dimethylamine had never been used as an unhairing agent, and only one type of glove was used, the straight finger, no. 6, glove. A third tannery was then visited, and it was discovered that here dimethylamine was not used, that both curved and straight finger gloves were being worn

and that leukoderma developed in workers who wore either kind of gloves for any length of time.

To ascertain whether this type of leukoderma occurred only in tanneries, the names of various manufacturing companies where these gloves were used were obtained from the jobbers of the gloves, and these factories were visited. These included factories where electrical apparatus and decalcomanias were manufactured, electroplating works and meat packing plants. In all of these plants the workers who wore this brand of glove were affected with leukoderma.

An important clue was obtained by the insurance company from the rubber company in a letter of June 29. In this it was stated that, whereas these gloves had been manufactured for years, in September 1937 the formula had been changed slightly by the addition of a certain material designed to improve the aging properties of the rubber.

The company was then visited, samples of the gloves were shown and samples of the aging material obtained. This was an antioxidant known under the trade name of agerite alba, which was said to be monobenzyl ether of hydroquinone, containing less than 1 per cent of unchanged hydroquinone. The commercial product is a light tan powder with an aromatic odor, melting at 115 to 120 C. and having a specific gravity of 1.26. The pure product is white, very slightly soluble in water, practically insoluble in petroleum hydrocarbons but soluble in alkalis and benzene and in rubber up to 2 per cent. It is said to be nontoxic on ordinary handling, is nondiscoloring in diffuse daylight and gives a minimum discoloration in direct sunlight. For these reasons it is recommended by the manufacturers for use in white and light-colored gloves. The other ingredients used in the manufacture of the gloves were as follows:

Smoked sheet rubber	100 parts
Chrome yellow	5 parts
Whiting	125 parts
Cumar	3 parts
Stearex beads	10 parts
A small amount of soapstone and agerite alba	0.5 parts

These ingredients are mixed in a mix mill, and the mixture is rolled into thin sheets. The sheets are cut up into small pieces and placed in metal drums containing petroleum naphtha. There are 7 parts of naphtha to 1 part of compounded rubber. The drums are revolved for about forty-eight hours, after which time the rubber is completely dissolved. The solution is then pumped into a storage tank, from which it is allowed to run into the dipping vats. Porcelain forms are dipped into the solution in the vats and allowed to remain for a short time. The rubber

depositing on the forms is allowed to dry, and then the forms are dipped repeatedly until the desired thickness of rubber is obtained. After drying, the rubber is cured (vulcanized) by immersion in a 4 per cent solution of sulfur monochloride in benzene. The gloves are again allowed to dry, taken off the forms and turned inside out, and the process is repeated. After this they are dusted with soapstone.

Samples of all of the ingredients used in the manufacture of these gloves were obtained from the rubber company, and the affected workers in tannery 1 were given patch tests. Ten men were tested with (*1*) chrome yellow, (*2*) stearex, (*3*) the antioxidant, (*4*) whiting, (*5*) soapstone, (*6*) cumar, (*7*) the antioxidant and (*8*) pieces of a new acid-cured rubber glove made by the rubber company. The patches were allowed to remain on for seven days. All of the workers except 1 reacted to patches 3 and 7. It is possible that this 1 may have lost the patch from under the adhesive plaster. There was a slight reaction to patch 8, a piece of rubber glove which contained only traces of the antioxidant.

On July 24, two weeks after the patches were applied, there were signs of leukoderma at the sites of the patch tests with the antioxidant in 5 of these workers. On Jan. 25, 1940, 8 of the 10 workers were seen, and 3 of them who had shown no leukoderma on July 24 now showed leukoderma at the site of the original antioxidant patch. At the same time areas of leukoderma produced by the patch test had been repigmented in 2 of the workers.

To determine whether the tanning liquors containing these chemicals had some effect on the ingredients in the rubber by producing new compounds and in this way causing leukoderma, pieces of the rubber glove used in patch test 8 were dipped into the various tanning liquors and applied as patch tests on 6 other workers who had leukoderma: (*1*) a 1 per cent solution of dimethylamine; (*2*) the actual unhairing solution of dimethylamine and lime (as this unhairing solution is strongly alkaline and therefore caustic, the alkalinity was reduced to p_H 11 by the addition of a few drops of sulfuric acid); (*3*) the tanning solution (a green liquid consisting of about 1.5 per cent of chromium sulfate and sufficient sulfuric acid to give it a p_H of 3.3), and (*4*) the liquid expressed from the leather taken out of the fat liquor drums and consisting of remnants of the various dyes and oils used in the fat-liquoring process.

These patches were taken off each day, and the skin was inspected. The patches were remoistened with the liquors and then reapplied for seven days. There was no reaction under any of the patches at the end of the week. Seven days later, one of the men, the janitor, had a mild reaction under each of the four patches. No leukoderma developed at the site of the reactions, showing that the tanning liquors apparently did

not act on the chemicals in the rubber gloves in such a way as to change their chemical composition and produce leukoderma.

To determine whether acid curing affected the action of the antioxidant and caused leukoderma, it was decided to make patch tests on all the workers with twelve samples of vulcanized rubber in its various stages of manufacture. The rubber company prepared these samples. By that time, however, it was evident that the antioxidant was the cause of the leukoderma, and the idea was dropped.

We felt, however, that tests should be made with hydroquinone, because Oettel [1] had performed experiments with it in connection with its contemplated use as a food preservative. During the course of these experiments he fed cats daily doses of hydroquinone and observed that among other changes of chronic hydroquinone poisoning there was depigmentation of the hair and black cats were temporarily changed into gray cats.

Patch tests were made on 4 of the tannery workers and 4 clinic patients, all Negroes, with a 20 per cent ointment of hydroquinone in benzoinated lard. No positive results were seen.

Twenty-five workers were then given patch tests with vulcanized rubber containing nothing but 1 per cent of the antioxidant. At the end of a week, the rubber patches were removed and 22 of the men were reexamined. Four of them showed positive reactions at the site of the rubber patches, and 1 of the 4 showed a desquamation of the skin underneath which was a definite area of leukoderma. In 1 of the 3 who did not have leukoderma at the time the patches were removed, leukoderma developed at the site of the test two weeks afterward. Two had ill defined leukodermic spots, and 2 showed brown scaling. On final examination, on Jan. 25, 1940, 12 of 19 of the original 25 workers given patch tests with the vulcanized rubber showed leukoderma at the site of the patch test.

In a second tannery the same experiments were performed on 4 workers. Patch tests were made with the unvulcanized rubber; an ointment of 20 per cent hydroquinone in benzoinated lard was rubbed into an area on the back, and a saturated solution of hydroquinone in ether was applied to a similar area. The rubber was kept in contact with the skin for seventy-two hours, and the ointment and the ether solution were applied for four days. There were no reactions, and no leukoderma developed in the patients treated with hydroquinone; but five months later 2 of the patients who had been given patch tests with the unvulcanized rubber showed areas of depigmentation at the site of the patch tests.

---

1. Oettel, H.: Die Hydrochinonvergiftung, Arch. f. exper. Path. u. Pharmakol. **183**:319-362, 1936.

Later 2 clinic patients were given a 20 per cent ointment of hydroquinone in benzoinated lard, and 2 patients were given a 20 per cent ointment of agerite alba in benzoinated lard; all were instructed to rub the ointment in thoroughly every night and then cover the anointed area with gauze. This was persisted in for six weeks, during which time the patients were inspected once a week. No dermatitis ensued, nor did leukoderma develop in the anointed areas. Two volunteers were then given a 50 per cent ointment of agerite alba. These patients rubbed a small amount of this ointment into one spot on their thighs for four weeks, covering the skin with a piece of gauze after each inunction. They were examined weekly for the first month and then biweekly for two months, but no dermatitis or leukoderma developed in either case.

Two volunteers were then given patch tests with agerite alba powder. A small amount was moistened, applied to a piece of gauze and strapped to a small area on the thigh. This patch was allowed to remain on the skin for a week, and at the end of the week a new patch was applied. At the end of two weeks the patch was permanently removed and the skin inspected. No dermatitis was present at that time, but two weeks later definite leukoderma began to appear; a week later the areas on 1 patient were definitely depigmented (fig. 5). In the case of the second patient leukoderma did not appear until four weeks after the removal of the patch.

The first patient was then given an ointment of 75 per cent agerite alba in hydrous wool fat. This was applied to a small area on the leg every night. In three weeks after beginning these applications the affected area was dry; the skin appeared shiny with slight desquamation, and there was partial depigmentation. One week later there was complete depigmentation in the area, and this has persisted to date (fig. 6).

The agerite alba powder was then dissolved in alcohol and collodion, and the solution was painted on one small area of the patient's left leg every night, the collodion from the previous painting being removed before the paint was reapplied. In two weeks there was the same glistening appearance of the skin at the tested site, and a slight amount of desquamation. There was no pruritus, but a week later definite depigmentation was seen.

These experiments showed that the antioxidant in rubber, in powder form, in alcohol, ether and collodion and in 75 per cent strength in an ointment base is capable of producing definite depigmentation of the skin if applied daily for two to four weeks. In 1 patient in the area treated with the powder the pigment began to show signs of returning in four to six weeks; in the other there was still some depigmentation after five months. It would also seem that the small percentage of hydroquinone present played no part in the depigmentary process.

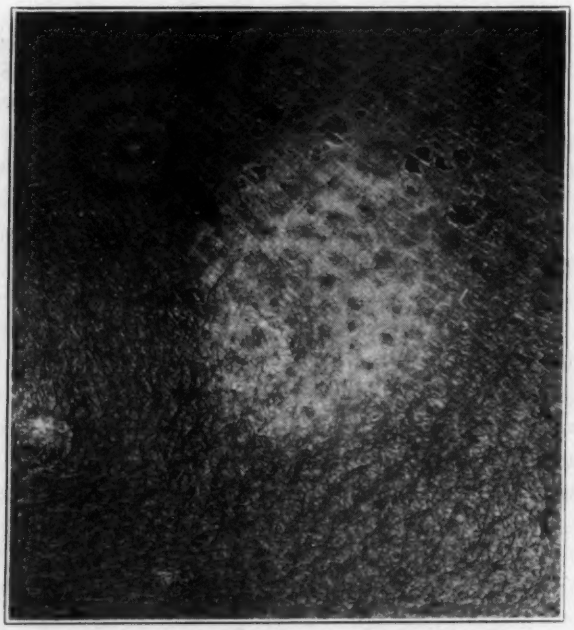


Fig. 5.—Positive result of a patch test with agerite alba in powder form.

Fig. 6.—Right leg tested with 75 per cent agerite alba in an ointment; left leg tested with 20 per cent agerite alba in an alcohol, ether and collodion mixture,

Fig. 7.—Repigmentation on Dec. 29, 1939.

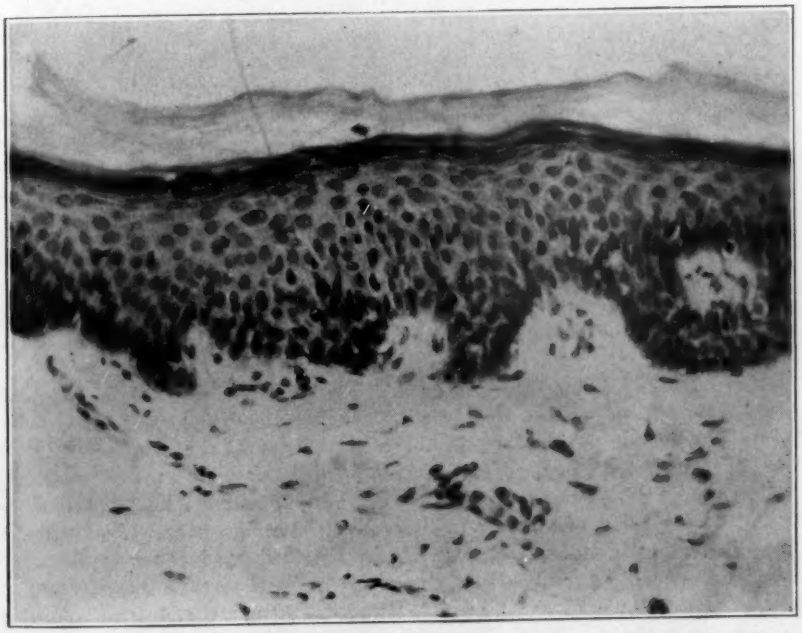


Fig. 8.—Repigmentation in leukodermic area (× 243).

Repigmentation in the affected areas began in nearly all of the depigmented workers shortly after they discontinued wearing the offending gloves, and when these patients were last seen repigmentation had progressed to a remarkable degree (fig. 7). In a few cases, however, it was slow. This may be another instance of personal susceptibility.

To determine whether the action of the drug on the skin was accompanied by any deleterious effects on the men's general condition, complete examinations of the blood, including reticulocyte counts and Wassermann and Kahn tests, were made for 18 patients. One Wassermann reaction was strongly positive, but other than this the results of examination of the blood were within normal limits.

Biopsy specimens were taken from the left arm, mostly from the upper margin of the affected areas, from 3 of the Negroes, 1 Mexican and 1 white man. Two specimens were taken from each person, one including normal and adjoining depigmented skin and the other including repigmented areas, particularly the follicles and the surrounding depigmented skin. These were stained with the ordinary stains and with the dopa reagent. A section of an area of repigmentation stained with the dopa reagent (fig. 9) was examined by Dr. Fred Weidman, who reported as follows:

> There is slight hyperkeratosis in one portion of the section. Acanthosis is negligible. Pigmentation is spotty in distribution and extreme in degree along a certain short extent of the epidermis. In the stratum corneum and in the stratum granulosum the pigment has tended to accumulate in a way that does not appear consistent with the amount of pigment in the basal layers, giving a distinctive appearance. In the deeply pigmented foci pigmentation is greatest in the basal cell layer, with marked hyperpigmentation in the chromatophores in the tips of the dermal papillae. In the less pigmented areas there is also hyperpigmentation in these chromatophores. In general, there is no marked hyperpigmentation in the basal cell layer. The localization or distribution of the pigment is utterly irregular, but even where the pigmentation is not heavy there are fine granules of pigment in the intercellular spaces. The dendritic cells are sharply outlined by powdery grains of pigment in their stellate processes, which extend far up into the epidermis. In all cases the pigment is extremely fine and powdery.
>
> Interpretation of the Pigmentation: The primary activity is in the chromatophores, which are present even around the sweat glands but are most abundant in the tips of the papillae and in the blood vessels of the subpapillary layer. The dendritic cells in the epidermis have engulfed this pigment, thus accounting for its transportation upward into the epidermis. A rather unusual phenomenon is this accumulation of pigment in the stratum granulosum and to a somewhat lesser extent in the stratum corneum. The basal cells themselves are not the site of this production of pigment. Pigmentation in the basal layer is due more to the intercellular location of the pigment. However, there are still small quantities of pigment in the cytoplasm. The corium has a diffuse tingeing of the collagen bundles in addition to the granules of pigment. In the sweat glands the cytoplasm of the secretory cells in particular, and to a less extent of the collecting ducts, contains excessively finely granular, powdery pigment. The nuclei are not com-

promised except where the pigment is particularly dense, in which case the nucleus is somewhat pyknotic. There are no hair follicles or sebaceous glands in this section. Even the involuntary muscle around the sweat tubule is stained a diffuse brown. The arrectores pilorum muscles and also the involuntary fibers in the vessel walls have escaped involvement. In the lumens of the sweat glands is a rather shreddy, diffusely brown tinted material with some granules. One peculiar feature is the "backing up" or retention in the stratum granulosum of the pigment.

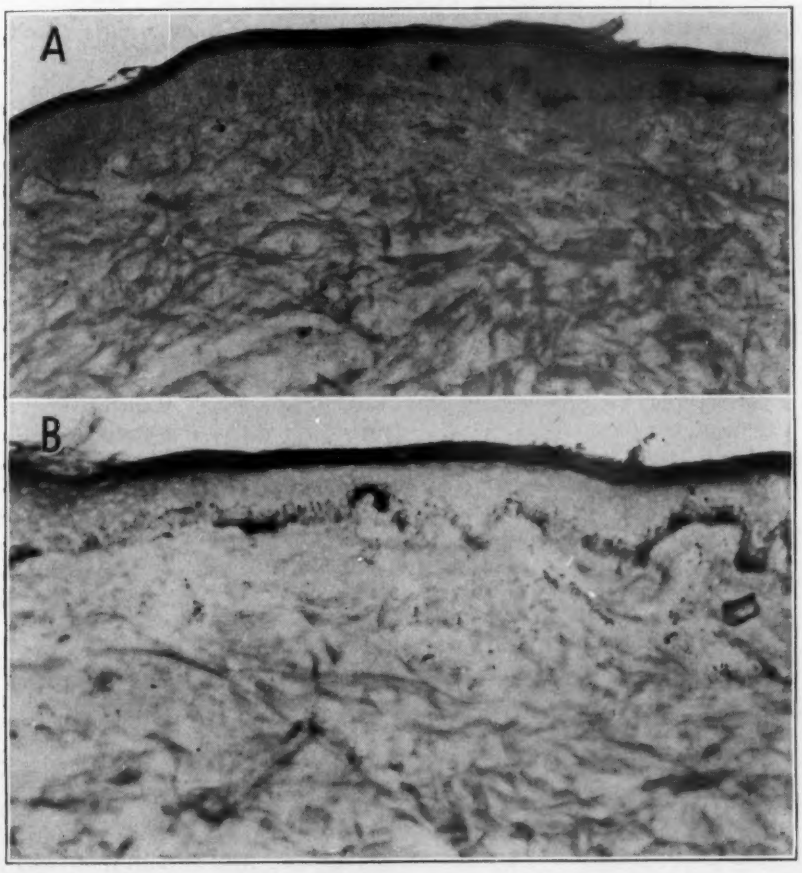


Fig. 9.—*A*, negative dopa reaction in depigmented skin (× 84). *B*, positive dopa reaction in repigmented skin (× 140).

A second section shows the same picture as the first, but the area of intense hyperpigmentation is more extensive. There is a lymphocytic proliferation around one blood vessel. There is a marked number of chromatophores in the tips of the derma papillae. The pigment is intercellular in the basal layer and is evidently located in the dendritic processes. The cells of the sweat gland give a positive dopa reaction, as noted in the first section, but there are no grains of pigment in these cells.

Summary: The melanin pigment is present in the chromatophores which occupy the dermal papillae and in the intercellular spaces of the basal layer of the epidermis. There are also small quantities of pigment within the cytoplasm of the basal cells. The dopa reaction brings out (in addition to the observations with hematoxylin and eosin staining) that the cells of the granular layer of the epidermis are dopa positive. There are dopa-positive granules in the stratum corneum and in the secretory cells of the sweat glands.

Several other sections of normal and of depigmented areas were examined by Dr. J. W. Miller, of the United States Public Health Service, who reported as follows:

Normal skin and area of leukoderma: Sections treated with dopa reagent show a rather sharp demarcation between the area of leukoderma and that of normal skin. There is a gradual decrease in the number of particles of pigment in the cells of the basal layer as the leukodermic area is approached. Dopa-positive particles occur in cells of the stratum granulosum and of the sweat glands, as intracellular and extracellular particles in the dermis and as isolated particles in the stratum corneum.

Dopa-positive particles are found in the pigmented basal cell layer of the normal portion of skin in the section. At the junction between the area of leukoderma and the normal skin there is a preponderance of dopa-positive particles in the last four or five cells before a sharp line of demarcation. Dopa-positive particles do not occur in the basal layer of the area of leukoderma, but they are noted in the dermis of the nonpigmented area, both isolated and some apparently in cells.

The same tissue stained with hematoxylin and eosin shows a similar sharp line of demarcation between the pigmented and nonpigmented cells of the basal layer, but the last few cells of the pigmented portions contain fewer particles of pigment than do the adjacent cells in the normal pigmented portion. Particles of melanin appear throughout the dermis in both portions of the section. Other than an absence of pigment, no pathologic changes are noted.

SUMMARY AND CONCLUSIONS

A peculiar leukoderma occurring among 20 men employed at a tannery who wore a heavy gauntlet type of rubber glove is reported.

After a thorough investigation, including patch tests of all the affected persons, it was discovered that an antioxidant added to the rubber for the purpose of improving its aging properties was the cause.

This antioxidant is known by the trade name agerite alba and is said to be the monobenzyl ether of hydroquinone.

Patch tests made on volunteer subjects with the rubber and with the antioxidant in powder form, in a 75 per cent ointment and in a 20 per cent solution of alcohol, ether and collodion gave positive reactions in 2 cases.

Tanning liquors played no part in the depigmentation, as investigation of all plants where this brand of gloves was worn showed the same type of leukoderma among the workers.

The action of the drug on the skin had no apparent effect on the general health of the persons, as the results of examinations of the blood were within normal limits.

Biopsy specimens of the depigmented and repigmented skin stained with the dopa reagent showed the dopa reaction to be negative in the depigmented areas and positive in the repigmented ones. There was no apparent injury to the cutaneous cells.

Repigmentation in many persons began soon after they ceased wearing the affected gloves.

Antioxidants have been used in rubber for many years, but never before has leukoderma been reported from the wearing of rubber goods. Therefore, it seems that monobenzyl ether of hydroquinone has a physiologic action on the skin that other antioxidants do not have. At present we are unable to say how this drug acts on the pigment of the skin. It apparently prevents the formation of melanin, either by action on the cells which form melanin or by action on one or more of the intermediate products in the formation of melanin from the aminoacid tyrosine. Since there is no definite evidence of damage to the cells, the latter theory seems the more likely.

ABSTRACT OF DISCUSSION

DR. LOUIS SCHWARTZ, Washington, D. C.: I should like to explain some of the uses of antioxidant in rubber and the reason they are used.

Rubber tends to deteriorate rapidly when exposed to the air; in other words, it combines with oxygen. It is a familiar fact that years ago stethoscope tubes turned hard and brittle. This was because antioxidants were not used in the manufacture. Rubber now lasts much longer than it used to, owing to the use of antioxidants.

Antioxidants, or age resisters, as they are called, are compounds which have such a strong affinity for oxygen that they are able to take up nearly all of the oxygen which ordinarily might combine with the rubber. In other words, the action of an antioxidant in rubber is to combine with whatever oxygen there may be in the rubber. Antioxidants will not prevent deterioration of rubber forever, but they will delay the process.

There are many antioxidants on the market, all labeled by different trade names. The trade name agerite alba, for instance, is one used by the Goodrich Tire and Rubber Company. Agerite is a part of the trade name that is applied to all of their antioxidants (probably fifteen or twenty compounds). Some are known as agerite white, some as agerite gel and some as agerite powder. The chemical name of agerite alba is monobenzyl ether of hydroquinone, a derivative of hydroquinone.

The mode of action of antioxidants in rubber is not well understood. One theory is that the antioxidant, having a stronger affinity for oxygen than has the rubber, becomes oxidized before the rubber. The fact that antioxidants in rubber lose their action after a time seems to substantiate this theory. Another theory is that, although the antioxidant takes up the oxygen to which the rubber is exposed, it rapidly gives it up in an inactive form. If this were entirely true, the action of the

antioxidant would last indefinitely. A third theory is that the mere presence of the antioxidant in the rubber prevents the oxidation of the rubber, although the antioxidant itself is not acted on. In other words, it acts like a negative catalyst. If this theory were so, the presence of the antioxidant would again prevent the rubber from deteriorating at all.

The fact that the antioxidant is used up in the rubber is proved by experiments which show that more antioxidant can be recovered from newly compounded rubber than from old rubber.

The products of oxidation of the ordinary antioxidants are dark-colored compounds, but the oxidation product of monobenzyl ether of hydroquinone is much lighter in color.

Rubber is tacky and cannot be used without being cured. The curing of rubber removes the tackiness and gives it proper stretch and the proper comeback from the stretch. Curing is done by heat or by chemicals. Heat can be applied in either dry form or moist. The chemical used is usually sulfur monochloride dissolved in benzene or in carbon disulfide. The heat cure does not affect the action of antioxidants on rubber, nor does it seem to affect their chemical composition. The acid cure, however, causes rapid changes of color with most antioxidants, because most antioxidants are attacked by active chlorine compounds. In other words, sulfur monochloride oxidizes the ordinary antioxidants. The acid cure, however, does not affect monobenzyl ether of hydroquinone as much as it does most other antioxidants and does not cause it to discolor. This is why this antioxidant is used in light-colored, acid-cured rubber goods.

Antioxidants have been used in rubber for many years, as Dr. Oliver has mentioned, but never before has leukoderma been reported from the wearing of rubber gloves. Therefore, it seems that either monobenzyl ether of hydroquinone has a physiologic action on the skin different from other antioxidants or other antioxidants do not act on the skin.

The reason that monobenzyl ether of hydroquinone causes leukoderma and that leukoderma has not been reported to have been caused by other antioxidants may be that this antioxidant is more soluble in water and, hence, more readily absorbed into the skin. It is freely soluble in alkalis. Most of the workers who had leukoderma from the wearing of rubber gloves worked with alkalis, and the antioxidant may have been dissolved from the rubber and allowed to come in contact with the skin in an absorbable state.

It was first thought that perhaps there was an excess of monobenzyl ether of hydroquinone in the rubber, which caused the excess to bloom out and come in contact with the skin and thus be absorbed. But an examination by competent rubber chemists of the rubber gloves containing it did not show any bloom.

It was then thought that perhaps the antioxidant was dissolved out of the rubber by the perspiration. To test this, a piece of the rubber glove containing monobenzyl ether of hydroquinone was soaked in water containing sufficient acetic acid to give the solution a p_H of 4; another piece of the glove was soaked in water containing a sufficient amount of alkali to give a p_H of 8, these being the limits of the range of the p_H of perspiration. It was found that after two weeks these solutions took 10 per cent of the monobenzyl ether of hydroquinone out of the rubber. This experiment showed that the perspiration, regardless of its p_H, could dissolve monobenzyl ether of hydroquinone out of the rubber. It is possible that this amount of the antioxidant, being absorbed into the skin, was the cause of the leukoderma.

DR. LEON H. WARREN, Washington, D. C.: My discussion will be limited to a few words on the identity of this chemical which possesses the unique property of producing depigmentation of the human skin on local application.

The monobenzyl ether of hydroquinone ($C_6H_5CH_2OC_6H_4OH$), or parahydroxyphenyl benzyl ether, consists of hydroquinone with the upper or prime hydroxyl group changed into an ether linkage, to which is attached the benzyl radical (a benzene ring with a CH_2 group). Since the monobenzyl ether has a free hydroxyl group, it has many of the properties of hydroquinone, yet, owing to its ether linkage, it is more stable, less easily oxidized and less soluble.

Hydroquinone ($C_6H_4[OH]_2$) is a benzene ring with two hydroxyl groups, one in the prime position and one opposite in the para position. One characteristic of hydroquinone is that it forms quinone on oxidation. Quinone is a six carbon ring but not a benzene ring (instead of having alternate double bonds all the way around the ring, quinone has only two double bonds—on opposite sides—with an oxygen at the bottom and at the top of the ring). The quinoid structure is responsible for the color in many colored compounds. The monobenzyl ether of hydroquinone, owing to the fact that the prime hydroxyl group is substituted, does not form quinone or quinoid compounds on oxidation.

Monobenzyl ether of hydroquinone is much more soluble in alkalis. This, together with the fact that perspiration becomes progressively more alkaline on standing on the skin, may explain why some of the reactions to patch tests, particularly to the agerite alba powder itself or incorporated in rubber, were much more effective than applications of the same antioxidant incorporated in an ointment base or in an ether solution.

DR. EVERETT C. FOX, Dallas Texas: This paper has interested me greatly, as has a previous publication (Oliver, E. A.; Schwartz, L., and Warren, L. H.: Occupational Leukoderma: Preliminary Report, *J. A. M. A.* **113**:927 [Sept. 2] 1939), because of a patient that I have had the opportunity of observing for some time. In November 1939 this patient had some gastrointestinal upsets and was given medication for amebiasis. He was started with carbarsone, an arsenical, and diodoquin, a quinone compound (5,7-diiodo-8-hydroxyquinoline). These were given in fairly large doses on alternate weeks for eight months.

After about two or three months the patient noticed some changes in the skin. A small area of vitiligo appeared about the collar button area. It rapidly increased and was three or four times the size before medication was discontinued. Another area of vitiligo developed on the shoulder, and an area, which had not previously been present, on the right cheek, 3 by 1 cm. During that same period the hair rapidly became gray, an effect comparable to that in the experimental work on the development of the gray cat. During the same time, thyroid was being administered because of a low metabolic rate.

After eight months all medication was discontinued. The vitiliginous areas gradually or fairly rapidly improved. The area on the cheek disappeared completely; the one on the shoulder was much smaller, and the one on the neck was back to its previous, original size and area of depigmentation.

About this time Dr. Oliver's first article was available, and I had considered the possibility that some of the drugs had produced the increase in vitiligo. Diodoquin is 5,7-diiodo-8-hydroxyquinoline, a closely related compound.

Herman (cited by Wise, L., and Sulzburger, M. B.: The 1939 Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1940, in an article on pigmentation changes in salamanders and trout, made this

observation: "The melanin content of the skin is diminished with the use of diiodotyrosine and diiodohydroquinone. These substances seem to influence the hormonal system."

The patient in question, requiring further medication, was given carbarsone only, and pigmentation did not recur. For the past six months the treatment has consisted of thyroid alone, and the pigmentation has not recurred.

DR. HENRY E. MICHELSON, Minneapolis: I merely want to heap some praise on Dr. Oliver and his co-workers because they have shown in this paper that busy, active practitioners can do research work equal to that done by laboratory workers.

DR. MARION B. SULZBERGER, New York: A little less than two years ago a group of manufacturers of bleaching or antifreckle creams asked me to perform studies on their bleaches. The manufacture and sale of bleaching creams represents a big industry. I was told that there are relatively few Negroes or Negresses who reach maturity without having tried to get a few shades lighter by the use of freckle creams. So the greatest use of these creams is not to reduce the degree of freckling but to bleach dark skins. There is a large export business in these products. A great deal is sold all over Africa, for example. Almost all the best known brands of antifreckle creams are manufactured in the South.

The basis of these creams is almost always some form of mercury. Many of them contain white ammoniated mercury in 5 to 15 per cent concentration. Some of the creams contain red mercuric oxide in somewhat lower percentage. The fact that throughout the dermatologic literature and dermatologic practice mercury is the most highly vaunted and the most used bleaching agent interested me in the project of scientifically studying the effects of these mercurials on the skin. Dr. Ludwig Schwarzschild and I carried out these studies on large numbers of Negroes.

At a meeting last year Drs. Oliver, Schwartz and Warren spoke to me about their observations with agerite alba. I then asked permission to include this substance as an extension of some of my studies of bleaching agents. The report I am now going to make is really made possible only through the courtesy of Dr. Oliver and his collaborators and is merely supplementary to their results.

One of the questions which arose, and which Dr. Oliver also mentioned, was whether the depigmentation from application of agerite alba was merely an effect of irritation. It seems to be a common belief that if pigmented skin is irritated sufficiently depigmentation is likely to occur. To check this, Dr. Schwartzschild and I applied agerite alba, full strength, to the skin of 18 Negroes. Simultaneously, to the skin of the same Negroes we applied ammoniated mercury, full strength, and hydroquinone, full strength, in each instance using just the powder moistened and applying it in patch tests. In all cases there was decided irritation from the full strength of each of the three substances. However, at the site of the irritation due to agerite alba in 17 of the 18 Negroes there was depigmentation after an average of twenty-seven and one-half days. At the site of the application of ammoniated mercury there was no change in pigmentation. This site, once the irritation had subsided, could not be distinguished from the normal surrounding skin. At the site of the irritation from hydroquinone, in 8 of 12 patients not only was there no depigmentation but there was decided hyperpigmentation.

I think that the conclusion to be drawn from this experiment is obvious: agerite alba does not act merely by producing irritation but exercises some specific damaging or inhibiting effect on the pigment or on the formation of pigment. More-

over, this specific effect is apparently not due to the presence of hydroquinone or simply to the irritation. The nature of this specific effect of agerite alba requires further study.

This work, of course, not only brings up many theoretic problems, such as new possibilities of studying the genesis of pigmentation and the origin of melanin and pigment but also suggests certain eminently practical problems.

It would, of course, be of great advantage to dermatologists to possess a reliable bleaching agent which could be used with safety in topical applications to produce any desired degree of local loss of pigmentation. With this objective in mind, Dr. Schwarzschild and I continued our studies, after corresponding with Dr. Oliver, who gave us several suggestions.

Our next experiment was designed to determine whether one could reduce the irritation and still produce the depigmentation. So we embodied the agerite alba in various vehicles, one of them being rubber cement. In a series of 7 Negroes, the 1 per cent agerite alba in rubber cement produced depigmentation in 4. However, there was still irritation. In other words, the conclusion is that we have not yet been able to discover an optimum concentration or a suitable vehicle by which no irritation would be produced and with which one could regularly elicit depigmentation.

In a third experiment, we tried the concentrated agerite alba and also pastes of 75 per cent agerite alba on the skins of 5 heavily freckled white persons. No effect was noted on the freckles.

In an extension of these experiments, we tried to find out whether the degree of depigmentation was parallel with the degree of irritation produced by the agerite alba. It was not. In 9 cases the irritation was seen first and later depigmentation appeared; in 8 depigmentation was seen before there was any clinically visible irritation, and in 1 case, in which the skin was severely irritated by the agerite alba in full strength, there was no depigmentation whatever.

I believe that our results, together with those of Drs. Oliver, Schwartz and Warren, now permit conclusions which can be stated approximately as follows:

1. The depigmentation produced by the local application of agerite alba is not simply the result of irritation but must be the result of some specific factor acting on the pigment or on the formation of pigment.

2. This effect is not due to the presence of free hydroquinone.

There is one more point I should like to bring up. In our experiments we were able to produce eczematous, allergic, specific sensitization both to the hydroquinone and to agerite alba, a real allergic sensitization, such as one can produce with poison ivy extracts. In approximately 50 per cent of the cases we produced this eczematous sensitization by the application of full strength agerite alba. Again, however, there was no definite parallelism between the sensitization produced and the depigmentation which followed. In other words, some of the persons who became sensitized did not become depigmented, and some who did not become sensitized did become depigmented.

I should like to compliment the presenters once again. It should be appreciated that, starting with a clinical observation, which was really at first based on a merely medicolegal and economic question, Drs. Oliver, Schwartz and Warren have, by their careful approach to the problem and by their scientific attitude, been able to bring to attention something which is new and fundamental. The importance of the discovery of this new and really effective bleaching agent is amply evident in the fact that this discussion has developed into a symposium on the genesis and

chemistry of pigment, including the practical applications of bleaching agents, the effects of rubber antioxidants and the relation of oxidation and reduction ferments to the mechanism of the formation of melanin and the genesis of pigment.

Dr. Samuel M. Peck, New York: I wish to congratulate the presenters on this interesting work. The most important point was that it has led to perhaps a new method of studying the oxidase reaction of the pigment. I, too, obtained clinically the same results which have just been reported. I was able to produce depigmentation in guinea pigs by local applications, but I was unable by feeding experiments to produce any changes such as have been reported as occurring in cats.

Technical difficulties were encountered in experimenting directly with frozen sections, because the dopa oxidase is destroyed by ether and alcohol, while agerite alba is practically insoluble in water.

It then occurred to me that the effect of agerite alba on the polyphenol oxidase in the leukocytes would lend itself well to direct experimentation, as this substance is less sensitive to alcohol and ether.

A number of years ago, Bloch and I published a method of demonstrating polyphenol oxidase by means of dopa (Bloch, B., and Peck, S. M.: Der Nachweis der Oxydase in den Zellen des myeloischen Systems durch 3, 4-Dioxy-phenylalanin, *Folia haemat.* **41**:166 [May] 1930), using this technic for fixation of blood smears. We experimented with the effect of agerite alba in such a preparation.

When a blood smear is exposed for one hour to ether prior to immersion in the dopa solution, according to the technic described by Bloch and myself, there is a negative dopa reaction in the leukocytes. It would then logically follow that if a fixed blood smear were exposed to a solution of agerite alba for one hour prior to immersion in a dopa solution, a negative reaction should ensue. However, when the blood smear, which has been previously fixed with formaldehyde vapor, is immersed in a 1 per cent solution of monobenzyl ether of hydroquinone for one hour, not only is a subsequent dopa reaction obtained, but it is much more strongly positive than the controlled dopa reaction. In collaboration with Dr. Harry Sobotka (to be published), I conducted many experiments on the various oxidase systems. They substantiated the observations that agerite alba seems to increase the polyphenolase oxidase even after it has been weakened by ether.

A number of allied hydroquinones were studied, such as the dibenzyl ether of hydroquinone, for their effect on the polyphenolase. There was none. Similarly these allied substances did not seem to act on animals as did the agerite alba.

The importance of these observations lies in the fact that the monobenzyl ether of hydroquinone seems to have a sharp specific antioxidase effect on the dopa oxidase, which differs from its effect on the polyphenolase. It also tends to point out the specificity of the dopa reaction. Agerite alba seems to be a specific dopa oxidase poison, and this information may throw a great light on the mechanism of vitiligo.

Dr. William Harvey Guy, Pittsburgh: This is a noteworthy communication because of the scientific explanation of a bizarre occupational dermatosis. The authors, I think, are to be particularly complimented on the fact that they have isolated the chemical at fault and have consulted the rather cooperative manufacturers with regard to changing the manufacturing process so as to avoid depigmentation in future contacts.

I have had the opportunity of studying 10 such cases in Pittsburgh. The condition occurred in car cleaners in the Pittsburgh Railway Company. They were referred without comment, for diagnosis and explanation. It was not suggested

at first that gloves might be in the background. It was first suspected that the cleaning materials that they used might be at fault. Definite reactions to patch tests could be produced but no depigmentation. Then, finally, the glove material was suspected. Patch tests with both used gloves and new gloves produced a mild erythema, usually appearing after the fourth day and more often at the end of a week. Depigmentation rarely appeared before fourteen days after the application.

A histologic section was made of tissue in the area of the positive reaction to the patch test, and rather intense edema, both parenchymatous and interstitial, was found, involving the epidermis, particularly noteworthy with reference to the basal membrane. It was difficult to note the line of demarcation between the cutis and the epidermis. Repigmentation ensued in practically all cases. But there is one point that I should like to ask Dr. Oliver and his co-workers about, and that is whether or not in their cases the repigmentation was complete. In our cases repigmentation did occur but it was not complete.

I think another point of interest and importance in connection with this presentation is the implications of the use of this antioxidant in dermatology from a practical standpoint in the future. If the substance produces permanent depigmentation, it may ultimately prove to be of some service in the removal of residual pigment, as after burns, for cosmetic results.

Dr. E. B. Tauber, Cincinnati: I want to report other types of cases. Since Dr. Oliver called my attention to this phenomenon about a year ago, I have come in contact with 4 additional cases, in which the condition had nothing to do with an occupational type of leukoderma. In 2 of these the conditions were approximately the same and were due to the rubber in dress shields. The third case was that of an obese woman who wore a rubber corset for reducing purposes and was depigmented to a decided extent after using the corset for a little less than a month. The fourth case was that of a Portuguese who had complained of pain in the buttocks and was told by his physician to apply heat; so he lay on a hot water bag for about three weeks, and a depigmented spot about the size of a palm appeared. Dr. Oliver has pictures of the 2 women. They were given patch tests with agerite alba and gave positive reactions. The obese woman and the Portuguese also gave positive reactions to patch tests with agerite alba in powder form.

There are so many other situations in which rubber comes in contact with the skin that I think one needs to be on the lookout for cases of this condition. Repigmentation has almost completely taken place in both women.

There is one fact which has not been mentioned. The depigmentation takes place in a sort of stippling way at first, and then the skin gradually becomes milky white. Repigmentation appears in the same way; little black spots come out and then fuse, and the skin finally becomes completely repigmented.

Dr. Fred D. Weidman, Philadelphia: I have been impressed with the remarkable consistency with which the skin around the hair becomes depigmented. In this connection, it appears that the commercialists have rendered us a great service, because they have unwittingly stumbled across a particular chemical—monobenzyl ether of hydroquinone—which is delicately specific in relation to the pigmentary oxidase. Thus, heretofore it was thought that oxidase was a single substance. However, it appears that the effect of this antioxidant is different on the cell processes from place to place.

As I see it, there are two possible explanations for this. One is that not simply one kind of oxidase is elaborated in cutaneous cells; perhaps there are

two different kinds, or perhaps even more, one of which (in perifollicular cells) is specifically affected by this particular compound while others are not.

There is one other possible explanation, namely, the factor of dosage. Around the hair follicles cellular processes in general are normally more active, and therefore larger quantities of oxidase, among other products, are produced in that position. These larger quantities are not "neutralized," so to speak, by the compound; whereas in positions apart from the follicles, where cellular processes are not so active, the oxidase is not produced so rapidly, and there is sufficient dosage of the compound to neutralize the oxidase. This, of course, is theoretic. No doubt the same thoughts have occurred to Dr. Oliver and his collaborators. But definite attention should be given to the consistency of the depigmentation around the hair follicles.

DR. GEORGE M. LEWIS, New York: I should like to ask Dr. Oliver if any of the patients have shown any constitutional symptoms or any toxic side effects.

DR. EDWARD A. OLIVER, Chicago: I appreciate the generous discussion. There is little that I can add to it.

Dr. Fox's observations are most interesting. He wrote me several months ago about his patient. While the depigmentation in his case may be only a coincidence, it is known from Oettel's experiments that hydroquinone taken internally has altered the color of hair.

Dr. Guy asked about repigmentation. In most of the cases there is repigmentation, but it is a partial, blotchy type of repigmentation. In tannery 1 there are as yet no cases of complete repigmentation, with the skin showing a normal type of pigmentation.

Dr. Lewis asked about constitutional symptoms. As far as we could see, there were no constitutional symptoms. The affected men never lost any time from work.

ULCERS OF THE LEGS IN SICKLE CELL ANEMIA

CLYDE L. CUMMER, M.D.
AND
CHARLES G. LaROCCO, M.D.
CLEVELAND

In dermatologic practice ulcers of the legs often present difficulty in differential diagnosis. A Negro patient in our outpatient clinic who had had several such ulcers for many months was finally found to have sickle cell anemia. To direct more general attention to this possibility is the purpose of our communication. It is necessary first to review briefly the clinical and hematologic picture of the blood anomaly.

Sickle cell anemia was first described by Herrick [1] in 1910. It was recognized early that while many of the Negro race show sickle cells in the peripheral blood—indeed, 7.8 per cent, according to Cardozo's [2] recent study—by no means all of this number are anemic. This has led to confusion in terminology. The anemia, first given Herrick's name, has been called sickle cell anemia and later drepanocytic anemia, while the terms sicklemia, meniscocytosis and drepanocytosis have been applied to the symptomless or nonanemic state. It is generally recognized, as has been noted by Diggs and Ching,[3] that the lines between nonanemic, mildly anemic and severely anemic conditions are not sharply drawn and that clinically conditions have been observed to pass from the sicklemia phase to the active phase and back again. Therefore, there has arisen the use of the terms latent and symptomless sickle cell anemia to denote the nonanemic phase.

The sickling trait is familial and apparently hereditary, dominant in character and transmitted according to the mendelian law. Syden-

---

From the Department of Dermatology and Syphilology, St. Vincent Charity Hospital.

Read at the Sixty-Third Meeting of the American Dermatological Association, Inc., Colorado Springs, Colo., May 30, 1940.

1. Herrick, J. B.: Peculiar Elongated and Sickle-Shaped Red Blood Corpuscles in a Case of Severe Anemia, Arch. Int. Med. **6**:517-521 (Nov.) 1910.

2. Cardozo, W. W.: Immunologic Studies of Sickle Cell Anemia, Arch. Int. Med. **60**:623-653 (Oct.) 1937.

3. Diggs, L. W., and Ching, R. E.: Pathology of Sickle Cell Anemia, South. M. J. **27**:839-845, 1934.

stricker [4] concluded that more children born of parents both of whom show meniscocytosis have sickle cell anemia than those born of 1 affected and 1 normal parent.

A striking feature of sickling is that it is limited almost exclusively to the Negro race. In fact, until recently it was regarded as being so limited. Sydenstricker [4] stated that it occurred only in Negroes or in those with a strain of Negro blood. However, Haden and Evans [5] regarded as authentic 8 examples of the disease in the white race. In each instance a careful examination had been made to exclude Negro blood. Later its occurrence in a Sicilian was reported by Pontoni.[6] Wallace and Killingsworth [7] tested 139 Mexican children and 100 Mexican adults and found the condition in 3. On the other hand, in an examination of 2,000 white persons Sydenstricker failed to find an instance of sickling.

Sickling has been observed at all ages from infancy to 78 years, but the incidence of anemia is highest in childhood. Progressive diminution with advancing age is accounted for by excessive mortality. There seems to be no preference as to sex, as shown by the compilation of published statistics made by Diggs, Ahmann and Bibb,[8] for in a group of 2,831 Negroes examined, 8.1 per cent of the females and 8.4 per cent of 2,252 males had the trait. There is no appreciable difference in percentage incidence in the United States between persons living in the northern and in the southern states.

CLINICAL FEATURES OF THE ANEMIC STATE

With meniscocytosis only there may be no symptoms or physical signs. With anemia the signs vary somewhat with the duration of the disease. In infants and young children there is malnutrition, and at the age of puberty retardation of development is often noted. The clinical manifestations have been described by Huck,[9] Diggs and co-workers,

4. Sydenstricker, V. P.: Sickle Cell Anemia (Herrick's Syndrome), in Christian, H. A., and Mackenzie, J.: Oxford Medicine, New York, Oxford University Press, 1930, vol. 2, pt. 3, pp. 849-860.

5. Haden, R. L., and Evans, F. D.: Sickle Cell Anemia in the White Race: Improvement in Two Cases Following Splenectomy, Arch. Int. Med. **60**:133-142 (July) 1937.

6. Pontoni, L.: Sulla eritropatia drepanocitica constituzionale tipo Herrick, Haematologica **20**:657-724, 1939.

7. Wallace, S. A., and Killingsworth, W. P.: Sicklemia in the Mexican Race. Am. J. Dis. Child. **50**:1208-1215 (Nov.) 1935.

8. Diggs, L. W.; Ahmann, C. F., and Bibb, J.: The Incidence and Significance of the Sickle Cell Trait, Ann. Int. Med. **7**:769-778, 1933.

9. Huck, J. G.: Sickle Cell Anaemia, Bull. Johns Hopkins Hosp. **34**:335-344, 1923.

Sydenstricker and co-workers and others. As with all anemic states, the patient's complaints include weakness and general poor health. In order of frequency Anderson and Ware [10] listed the following signs and symptoms: greenish yellow scleras, heart murmurs, enlargement of the liver, adenopathy, abdominal pain, enlarged heart, ulcers of the leg, pulmonary disease, fever, enlarged spleen, vomiting and infantile genitalia. Adenopathy occurs chiefly in the cervical and axillary lymph nodes. Since the complaints may include pains in the joints and muscles (often regarded as rheumatism), shortness of breath and palpitation, the mistaken diagnosis of "heart disease" is occasionally made; or in the mind of the physician the joint and cardiac symptoms may be correlated and explained as evidences of rheumatic infection.

The green discoloration of the scleras frequently encountered must not be confused with the yellow of biliary jaundice or the muddy pigmentation often seen in Negroes. However, clear scleras cannot be regarded as conclusive evidence against the coexistence of sickling, since in a series of 97 Negroes with no definite scleral discoloration, Diggs, Ahmann and Bibb found sickle cells in the blood of 6.

Enlargement of the heart may be associated with a systolic apical murmur. The splenic enlargement is occasionally enormous, but there is a tendency toward atrophy as the disease advances, sometimes to such an extent that the mere remnant is not discoverable at splenectomy. The legs may show edema; ulcers and scars will be described later.

Recurrent attacks of acute abdominal pain occur not infrequently and have been emphasized by many writers on the subject, including Leivy and Schnabel.[11] As described by Campbell,[12] these episodes may be severe and accompanied by obstructive jaundice, fever, muscle spasm, leukocytosis, nausea and vomiting, simulating cholecystitis, appendicitis, salpingitis or ileus. Severe attacks of pains in the joints or bones may suggest acute osteomyelitis or acute rheumatic fever. Occasionally there is low grade fever.

Cerebral vascular accidents have been reported, and Bridgers [13] stated that the disorder may manifest itself first by signs and symptoms indicative of cerebral vascular disease, leading to a diagnosis of either thrombosis or intracranial hemorrhages.

---

10. Anderson, W. W., and Ware, R. L.: Sickle Cell Anemia, J. A. M. A. **99**:902-905 (Sept. 10) 1932.

11. Leivy, F. E., and Schnabel, T. G.: Abdominal Crises in Sickle-Cell Anemia, Am. J. M. Sc. **183**:381-391, 1932.

12. Campbell, E. H., Jr.: Acute Abdominal Pain in Sickle Cell Anemia, Arch. Surg. **31**:607-621 (Oct.) 1935.

13. Bridgers, W. H.: Cerebral Vascular Disease Accompanying Sickle Cell Anemia, Am. J. Path. **15**:353-362, 1939.

Active sickle cell anemia appears to have a definite effect on the fertility of the female, according to Sodeman and Burch,[14] for pregnancy is seldom reported in cases of the disease. They listed 1 case of their own in which the patient reached term and the baby's blood showed sicklemia when first examined, six weeks after birth, and 2 other cases, previously reported by Lash [15] and Sharp and Schleicher,[16] in which live, full term babies were delivered. Indeed, sickle cell anemia has been regarded as a possible cause of abortions.[17]

PATHOLOGIC CHANGES

The following essential pathologic changes were summarized by Diggs and Ching: [3] sickled erythrocytes, congestion of the capillaries, thrombi, infarcts, fibrosis, hemolytic anemia with increased phagocytic activity of the reticuloendothelial system, retention jaundice, deposits of pigment in the liver, spleen, bone marrow, lymph nodes and kidney, hyperplasia of the bone marrow, a regenerative blood picture and degenerative visceral changes. Other changes in the tissue regarded by them as noteworthy are early splenic congestion, followed by hemorrhage, infarction and fibrosis with siderotic nodule formation and late atrophy, hepatomegaly with prominent Kupffer cells, congestion, pigmentation and scarring of the kidney, cardiac enlargement, ulcers of the legs and osseous changes.

The heart is frequently hypertrophic, the hypertrophy being confined to the left side, predominantly in the left ventricular wall, and the myocardium may show slight to moderate patchy degeneration, according to Steinberg,[18] who made an extensive review of the pathologic studies.

Bridgers [13] observed that in 1 of his cases of cerebral vascular accidents the large subarachnoid vessels had undergone gradual obliteration, with final complete closure through a process identical with that which results in occlusion of the splenic arteries, while in the other the process developed in connection with the small intracerebral vessels, resulting in multiple focal necroses and hemorrhages in the brain. Diggs and

---

14. Sodeman, W. A., and Burch, G. E.: Pregnancy in Active Sickle Cell Anemia, New Orleans M. & S. J. **90**:156-158, 1937.

15. Lash, A. F.: Sickle Cell Anemia in Pregnancy, Am. J. Obst. & Gynec. **27**:79-84, 1934.

16. Sharp, E. A., and Schleicher, E. M.: Hemologic Observations on Sickle Cell Anemia, Am. J. Clin. Path. **6**:580-590, 1936.

17. Lewis, A. W., Jr.: Sickle Cell Anemia with Pregnancy, Am. J. Obst. & Gynec. **33**:667-671, 1937. Yater, W. M., and Mollari, M.: The Pathology of Sickle Cell Anemia: Report of a Case with Death During an "Abdominal Crisis," J. A. M. A. **96**:1671-1675 (May 16) 1931.

18. Steinberg, B.: Sickle Cell Anemia, Arch. Path. **9**:876-897 (April) 1930.

Bibb,[19] having found the small blood vessels distended by sickled cells, advanced the theory that the great length of these cells interferes with the free circulation of the blood and that this is a factor in the production of thrombosis, a common feature in this disease.

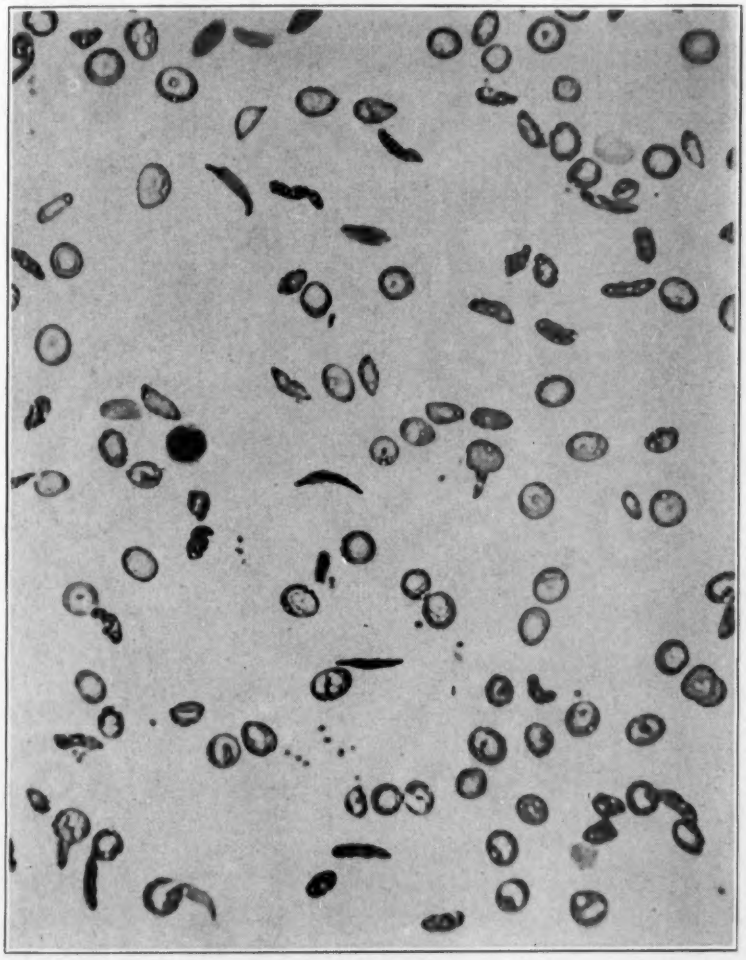


Fig. 1 (case 3).—Blood film, stained with Wright's stain, showing paucity of erythrocytes, poikilocytosis, increased central pale area and occasional elongated and sickle-shaped red corpuscles (× 510).

The bone in many instances shows evidence of degenerative and reparative processes in the marrow, the lesions including thrombosis, infarction, necrosis, hemorrhage, granular and crystalline deposits, hya-

19. Diggs, L. W., and Bibb, J.: The Erythrocyte in Sickle Cell Anemia, J. A. M. A. **112**:695-701 (Feb. 25) 1939.

linization, fibrosis, abnormal calcification and new bone formation, according to Diggs, Pulliam and King.[20] They stated that the changes in the skull usually described as characteristic include increased thickness, absence of a well defined outer table, osteoporosis and pointed trabecular striations radiating outward from the inner table and perpendicular to it, an abnormality not specific for sickle cell anemia, since it may be found also in erythroblastic anemia, hemolytic jaundice and other conditions. The bones of the extremities most likely to show abnormalities are the tibia and the fibula.

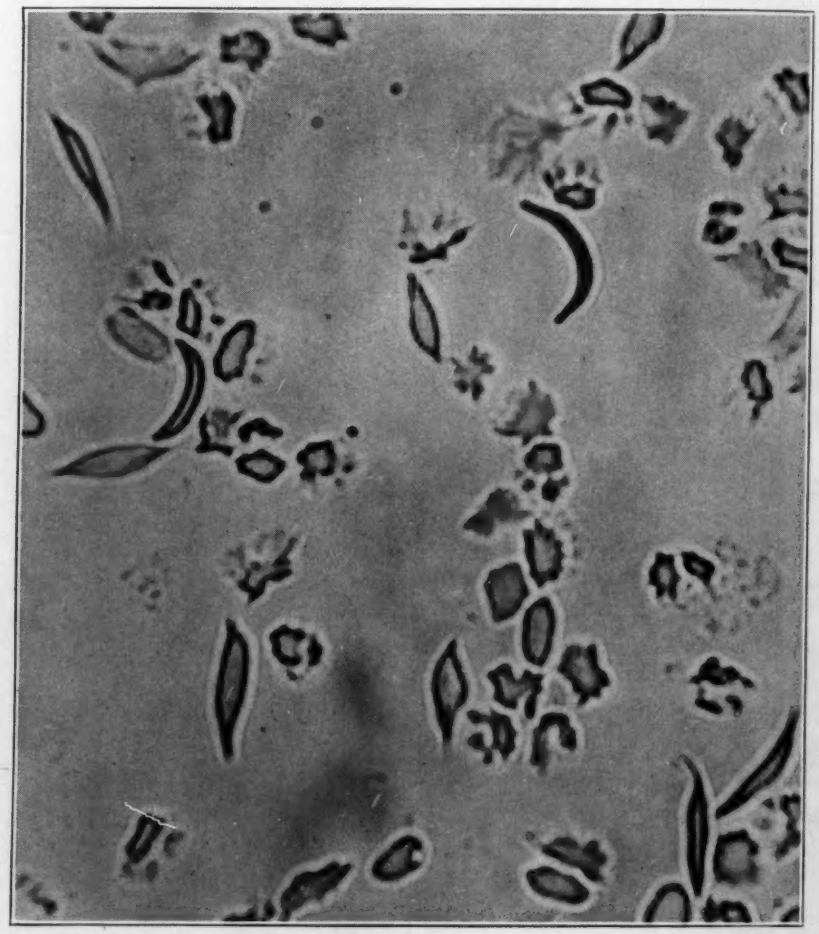


Fig. 2 (case 3).—Wet blood smear, sealed with petrolatum, after standing twenty-four hours, showing crescentic and oat-shaped forms (× 945).

20. Diggs, L. W.; Pulliam, H. N., and King, J. C.: The Bone Changes in Sickle Cell Anemia, South. M. J. **30**:249-259, 1937.

THE BLOOD PICTURE

It was the striking appearance of the erythrocytes which first drew attention to this anomaly. The morphologic changes are best observed when a drop of blood is sealed under a cover slip and studied for hours or even days. While occasionally slender, pointed or sickle-shaped cells

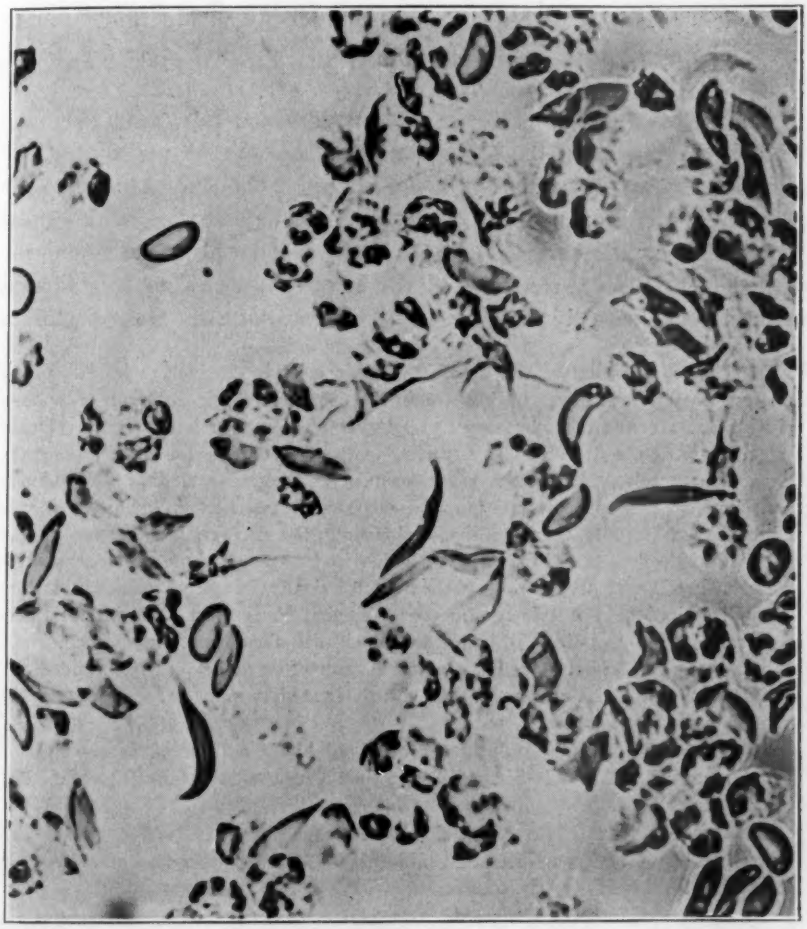


Fig. 3 (case 3).—Wet blood smear, sealed with petrolatum, after standing forty-eight hours, showing elongated and multipointed forms (× 920).

are seen when the preparation is first made, usually time is required for the development of characteristic shapes. The behavior of the erythrocytes in wet preparations has been fully described by Diggs and Bibb.[19] While the change in the erythrocytes may begin in the first hour after the blood is obtained, usually it takes place at maximal rate in from two to six hours, and often it is complete within twelve to twenty-four

hours. Erythrocytes in stained blood films resemble those found in newly made moist preparations. Fish fin or multipointed shapes are not usually seen in stained films in complete form but are occasionally found on careful search.[21]

The blood has been studied by numerous investigators, including Emmel,[22] Sydenstricker, Mulherin and Houseal,[23] Huck,[9] Hahn and Gillespie,[24] Hein, McCalla and Thorne,[25] Graham and McCarty,[26] Sharp and Schleicher,[16] Vaubel,[27] Haden and Evans [5] and, most recently, Diggs and Bibb.[19]

In Diggs's [28] series of 72 cases the red blood cell count averaged 2,600,000 per cubic millimeter and the hemoglobin 45 per cent. The reticulocyte count was usually elevated, often about 25 per cent, the percentage increasing during exacerbation and decreasing with remission, following the curve of the nucleated blood cells. He found the white blood cell count characteristically increased, the average in 69 cases being 18,000 per cubic millimeter. The resistance of erythrocytes to

---

21. The examination of the blood for sickle cells is extremely simple. While hanging drop preparations of blood mixed with physiologic solution of sodium chloride are recommended by some, every practical purpose is served by placing a small drop of blood on a slide, covering with a thin cover slip and rimming the edges with petrolatum. Such preparations may be kept several days for observation. Sealing prevents evaporation and consequent degenerative changes in the red cells and permits them to live, exhausting the oxygen and increasing the carbon dioxide content in the plasma, which in turn accelerates the morphologic changes. Fresh wet preparations should be practically free from rouleaux formation and crenation. For this reason the slides and cover slips must be absolutely free from grease and lint. It is helpful to cleanse them immediately before use with 95 per cent alcohol to which a small amount of ammonia has been added and to dust them off with a camel's hair brush immediately before picking up the drop of blood.

22. Emmel, V. E.: A Study of the Erythrocytes in a Case of Severe Anemia with Elongated and Sickle-Shaped Red Blood Corpuscles, Arch. Int. Med. **20**: 586-598 (Oct.) 1917.

23. Sydenstricker, V. P.; Mulherin, W. A., and Houseal, R. W.: Sickle Cell Anemia: Report of Two Cases in Children with Necropsy in One Case, Am. J. Dis. Child. **26**:132-154 (Aug.) 1923.

24. Hahn, E. V., and Gillespie, E. B.: Sickle Cell Anemia: Report of a Case Greatly Improved by Splenectomy; Experimental Study of Sickle Cell Formation, Arch. Int. Med. **39**:233-254 (Feb.) 1927.

25. Hein, G. E.; McCalla, R. L., and Thorne, G. W.: Sickle Cell Anemia, with Report of a Case with Autopsy, Am. J. M. Sc. **173**:763-772, 1927.

26. Graham, G. S., and McCarty, S. H.: Sickle Cell (Meniscocytic) Anemia, South. M. J. **23**:598-607, 1930.

27. Vaubel, E.: Die Sichelzellenanämie, Ergebn. d. inn. Med. u. Kinderh. **52**: 504-542, 1937.

28. Diggs, L. W.: The Blood Picture in Sickle Cell Anemia, South. M. J. **25**:615-620, 1932.

hypotonic solution of sodium chloride is variable but usually increased. The average of determinations in 25 cases of active involvement revealed hemolysis beginning in a 0.35 per cent solution of sodium chloride and complete hemolysis in a 0.22 per cent solution, although extremely low percentages have been reported by Bell, Kotte, Mitchell, Cooley and Lee [29] and one of 0.03 per cent by Hahn.[30] The hemolytic character of the anemia is confirmed by finding an increase in the serum bilirubin. The direct van den Bergh test usually gives a negative result, and the indirect, a positive result. Urobilin is present in the urine.

TREATMENT OF ANEMIA

There is no known effective treatment for sickle cell anemia. There is no response to iron or liver therapy. Splenectomy was first suggested by Sydenstricker.[31] Ching and Diggs [32] reviewed the results in reported cases and concluded that permanent benefit following the procedure had not been proved. Haden and Evans [5] followed 2 patients for fourteen and five years, respectively, after surgical treatment but found it difficult to evaluate the efficacy of splenectomy.

ULCERS OF THE LEGS

In the first report on a patient with sickle cell anemia Herrick [1] described scars on the legs, which were said to have followed yaws, the patient having formerly resided in the West Indies. However, even on arrival in New York years afterward the patient had a sore on one ankle which left a similar scar. In the next 3 cases reported, respectively, by Washburn,[33] Cook and Meyer [34] and Mason [35] there were ulcers of the legs. Since then the occurrence of such ulcers in this condition has been noted by many in the general medical literature.

---

29. Bell, A. J.; Kotte, R. H.; Mitchell, A. G.; Cooley, T. B., and Lee, P.: Sickle Cell Anemia: Report of Two Cases in Young Children in Which Splenectomy Was Performed, Am. J. Dis. Child. **34**:923-933 (Dec.) 1927.

30. Hahn, E. V.: Sickle-Cell (Drepanocytic) Anemia with Report of a Second Case Successfully Treated by Splenectomy and Further Observations on the Mechanism of Sickle-Cell Formation, Am. J. M. Sc. **175**:206-217, 1928.

31. Sydenstricker, V. P.: Sickle Cell Anemia, South. M. J. **17**:177-183, 1924.

32. Ching, R. E., and Diggs, L. W.: Splenectomy in Sickle Cell Anemia: Report of a Case with Necropsy in an Adult on Whom Splenectomy Was Attempted, Arch. Int. Med. **51**:100-111 (Jan.) 1933.

33. Washburn, R. E.: Peculiar Elongated and Sickle-Shaped Red Blood Corpuscles in a Case of Severe Anemia, Virginia M. Semi-Monthly **15**:490-493, 1910-1911.

34. Cook, J. E., and Meyer, J.: Severe Anemia with Remarkable Elongated and Sickle-Shaped Red Blood Cells and Chronic Leg Ulcer, Arch. Int. Med. **16**:644-651 (Oct.) 1915.

35. Mason, V. R.: Sickle Cell Anemia, J. A. M. A. **79**:1318-1320 (Oct. 14) 1922.

Steinfield and Klauder [36] reported the condition in a Negress 38 years old, but reports by dermatologists have been conspicuously few. Occasionally in recent years patients have been presented at meetings of local dermatologic societies: 1 by King [37] (Philadelphia), 1 by Netherton [38] (Cleveland), 1 by Schwartz [39] (Cleveland), 2 sisters by Schwartz [40] (Cleveland), 2 by Cummer and LaRocco [41] (Cleveland) and 1 by Krugh [42] (Pittsburgh).

REPORT OF CASES

The following cases have been observed in our service at St. Vincent Charity Hospital. The first will be described in detail; the others, more briefly.

CASE 1.—W. M. G., a Negress aged 18,[43] was admitted to the medical division of the outpatient department on Dec. 22, 1933, complaining of "tired feeling" and pains in the joints. She had been seen in the surgical division at various times because of pains in the joints. The heart was enlarged, and there was a mitral systolic murmur. A diagnosis of compensated rheumatic heart disease was made. She reported at the dispensary at intervals, usually complaining of pains in the joints.

---

36. Steinfield, E., and Klauder, J. V.: Sickle-Cell Anemia, M. Clin. North America **10**:1561-1576, 1927. This description is the first one we have been able to find by dermatologists.

37. King, A. D.: Sickle Cell Anemia, Arch. Dermat. & Syph. **33**:756-757 (April) 1936.

38. Netherton, E. W.: Sickle Cell Anemia with Ulcer of the Leg, Arch. Dermat. & Syph. **34**:158-159 (July) 1936.

39. Schwartz, W. F.: Sickle Cell Anemia Associated with Ulcers on the Legs, Arch. Dermat. & Syph. **37**:866-867 (May) 1938.

40. Schwartz, W. F.: Ulcers of the Leg, Associated with Sickle Cell Anemia, in Sisters, Arch. Dermat. & Syph. **38**:1006-1007 (Dec.) 1938.

41. Cummer, C. L., and LaRocco, C. G.: Two Cases of Chronic Ulcers of Legs in Patients with Sickle Cell Anemia, Arch. Dermat. & Syph. **39**:168-170 (Jan.) 1939; at the second presentation of 1 of these cases (Cummer, C. L., and LaRocco, C. G.: Ulcers on the Legs in Sickle Cell Anemia, ibid. **40**:459-460 [Sept.] 1939) it was felt that the weight of evidence, especially the observation of a few giant cells and epithelioid cells in small tubercle formation, favored the diagnosis of tuberculosis. Although we feel that the argument is not entirely convincing, especially in view of the history of repeated complete healing followed by breaking down on numerous occasions, nevertheless there is enough room for reasonable doubt so that the diagnosis in this case should be revised.

42. Krugh, F. J.: Sickle Cell Anemia: Ulcer on the Leg, Arch. Dermat. & Syph. **40**:656 (Oct.) 1939.

43. We presented this patient at a meeting of the Cleveland Dermatological Society on March 24, 1938.[41] In discussion at this time attention was called to scars in the cervical region as suggesting the possibility of old tuberculosis. However, later questioning established the fact that the scars resulted from enlarged glands following osteomyelitis of the jaw from an infected tooth at the age of 12 years.

On March 13, 1936 she was seen in the surgical division with an ulcer on the leg. This had started as a pimple, which had been scratched. In spite of negative results of serodiagnostic tests, syphilis was considered, and intramuscular injections of bismuth subsalicylate were given. During this treatment there was temporary healing, followed by the breaking down of ulcers and the appearance of new ones. In November the Wassermann and Kline reactions were again negative, and numerous deep, irregularly shaped ulcers with arcuate configuration were found on the legs.

On Oct. 26, 1937 it was found that her second child, 2 years old, had been admitted to the University Hospitals of Cleveland about three months previously and had had a splenectomy for sickle cell anemia. The patient was referred to the wards of the hospital for study on March 7, 1938. The pupils were round, regular in outline and equal and reacted to light and in accommodation. The heart

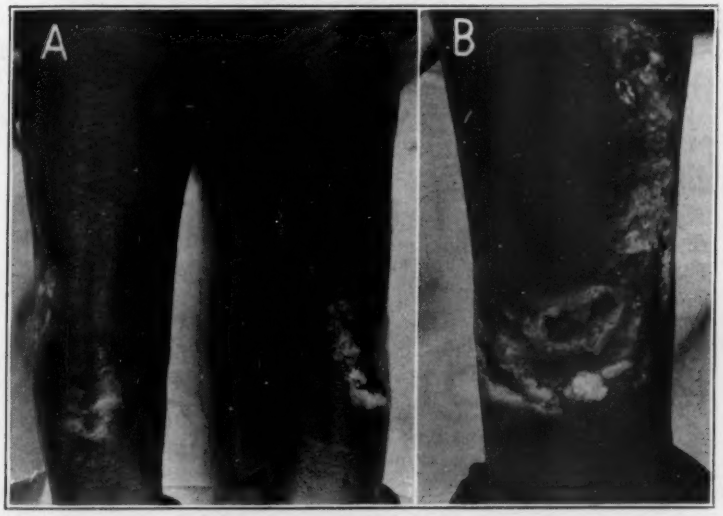


Fig. 4 (case 1).—*A*, ulcers of the legs, showing bilateral and symmetric arrangement. *B*, large ulcer showing irregularly arcuate outline.

had a mitral murmur but was well compensated. The lungs were clear, and the abdomen showed no masses or tenderness. The spleen was not palpable. Ulcers were still present on both legs above the ankles. They were deep, irregular in outline, some several inches across, with sluggish bases.

The urine was normal. A blood count showed 4,100,000 red blood cells and 8,000 white blood cells per cubic millimeter and 70 per cent hemoglobin. The differential count showed polymorphonuclear neutrophils 67 per cent, small mononuclear leukocytes 24 per cent, large mononuclear leukocytes 6 per cent, transitional forms 4 per cent and eosinophils 2 per cent. Sickle cells were found in wet preparations. The Wassermann and Kline reactions were negative. The icteric index was 3.5.

The following report was made by Dr. D. J. Rehbock after histologic examination of a section from the edge of one of the ulcers: "The section shows skin only at the margin of the tissue, and at the margin the skin has a relatively

normal appearance, there being only a small amount of lymphoid infiltration in the corium. The epithelial surface ends abruptly at the margin of the ulcer. The ulcer is covered with projecting masses of granulation tissue, beneath which is dense fibrous connective tissue heavily infiltrated with small mononuclear and polymorphonuclear cells. In several areas are multinucleated giant cells, but there are no typical tubercle formations. The underlying fat shows no changes. The pathologic diagnosis is chronic granulomatous inflammation of the skin with ulceration."

Roentgenologic examination showed that the skull, vertebrae and fibulas were normal, with no changes suggestive of sickle cell anemia.

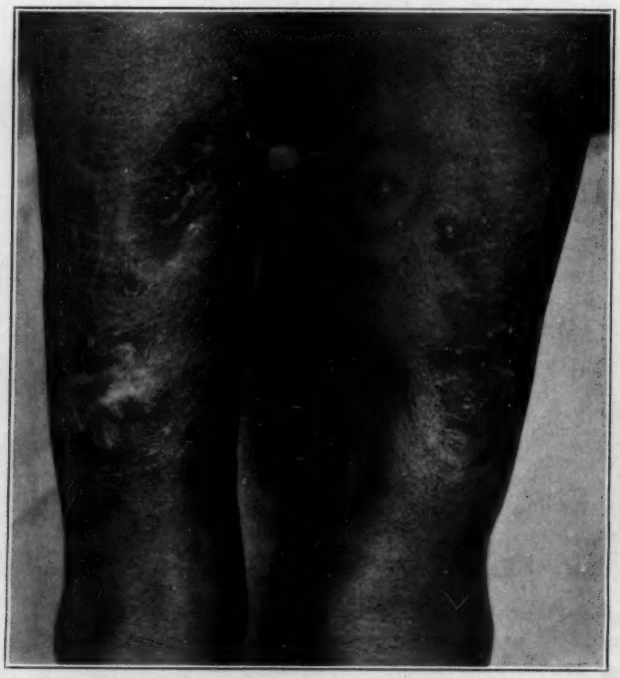


Fig. 5 (case 1).—Resulting scars. The ulcers were not healed until the end of two and a half years.

Local treatment of the ulcers consisted of mild antiseptic applications, such as boric acid ointment. Pills of ferrous carbonate U. S. P. were given internally. After a duration of over two years improvement with partial healing was noted in April 1938. Healing was complete in August 1938, and there has been no recurrence to the time of writing. On Nov. 7, 1938 examination of the blood showed 4,350,000 red blood cells and 10,400 white blood cells per cubic millimeter and 96 per cent hemoglobin. The differential count showed polymorphonuclear neutrophils 86 per cent, lymphocytes 12 per cent and eosinophils 2 per cent. A considerable proportion of sickle cells were found in wet preparations allowed to stand, although there were none in fresh preparations.

Summary.—In a Negress multiple ulcers of the legs appeared at the age of 21 years and required two and a half years for healing. Examinations of the blood showed sicklemia, anemia of moderate degree and negative Kline and Wassermann reactions. Biopsy material from an ulcer showed chronic granulomatous inflammation of the skin with ulceration. Roentgenograms of the skull, vertebrae and fibulas were normal. Antisyphilitic treatment did not influence the course of the ulcers. Signs and symptoms included clear scleras, pains in the joints, malaise, cardiac enlargement and systolic precordial murmur. The spleen was not palpable. The patient's daughter had had a splenectomy for sickle cell anemia.

CASE 2.—D. J., a Negress, had multiple ulcers of the right leg which appeared in 1937 when she was 13 years old.[44] First there was a single lesion on the right shin. This had been scratched and became crusted. About a dozen other lesions appeared. The secondary lesions could have been interpreted as impetiginous, probably having spread from infection of the original lesion.

There was a history of attacks in which the patient had a greenish tint of the scleras. The Wassermann and Kline tests gave negative results. Reactions to

Fig. 6 (case 2).—Atrophic scar with hyperpigmentation of border.

tuberculin tests were negative. Biopsy material showed chronic ulcer with no specific changes. Signs and symptoms included cardiac enlargement, systolic precordial murmur and frequent attacks of pain in the head, joints and extremities. The spleen and liver were not enlarged.

Histologic examination showed that the epithelium over the tissue adjacent to the ulcer was normal. Near the edge of the ulcer the papillae were broader and extended down more deeply. Here the corium showed much new connective tissue and many capillaries and was infiltrated with lymphoid and plasma cells. The base of the ulcer was covered with granulation tissue in which sickle cells were rather numerous. There was no apparent increase in fibrous tissue beneath the ulcer. Giant cells were not seen. There were no changes in the walls of the blood vessels. Examinations of the blood at various times showed severe anemia, sicklemia and other changes compatible with sickle cell anemia. Red blood cells ranged on three examinations from 2,200,000 to 2,340,000 per cubic millimeter; the leukocytes numbered 16,100 per cubic millimeter, and the hemoglobin amounted to 60 per cent. Sickled red blood cells were found on two occasions. The differential count of leukocytes showed polymorphonuclear neutrophils

44. Presented at a meeting of the Cleveland Dermatological Society on Sept. 30, 1937 by Dr. W. F. Schwartz.[39]

56 per cent, lymphocytes 31 per cent, monocytes 6 per cent and eosinophils 7 per cent. The resistance of the red cells to hypotonic solution of sodium chloride was increased. With the normal control hemolysis began with a 0.46 per cent solution and was complete with a 0.38 per cent solution, while the patient's blood showed beginning hemolysis with the 0.40 per cent solution and was not entirely complete even with the 0.28 per cent solution. The icteric index was 10. The sedimentation rate was 2 mm. in one hour, not corrected for anemia.

CASE 3.—R. F., a Negress aged 15, had a circular, depressed, smooth scar on the leg. The history indicated that at the age of about 4 years there had been an ulcer on the leg, which had lasted months. Examination of the blood showed severe anemia, with observations compatible with sickle cell anemia. The signs and symptoms included green scleras, severe pains in the joints, weakness, cardiac enlargement, arrhythmia and a precordial cardiac murmur. The spleen was not enlarged.

The Wassermann and Kline reactions were positive, but healing had taken place without antisyphilitic treatment. Examination of the blood showed: red blood cells, 2,610,000 per cubic millimeter; hemoglobin, 38 per cent; leukocytes, 12,800 per cubic millimeter; polymorphonuclear neutrophils, 68 per cent; small lymphocytes, 22 per cent; monocytes, 4 per cent, and transitional forms, 6 per cent. Crescent-shaped erythrocytes were found. The reticulocytes ranged from 0.4 to 0.6 per cent. The icteric index was 100 on one occasion and 26.5 five days later. In the test for resistance to hypotonic solution of sodium chloride, hemolysis began with the 0.34 per cent solution and was complete with the 0.28 per cent, while in tests of the normal control it began with 0.44 per cent and was complete with 0.40 per cent. The urine was normal, and there was no urobilin. Examination of the sternal marrow showed about the same percentage of sickled cells as in the blood. There was some increase in the number of normoblasts and erythroblasts. No change was noted in the white blood cells. The spinal fluid had a pressure equal to 110 mm. of water; it was clear, of normal color, showed 40 cells per cubic millimeter and gave a negative reaction to the gum mastic test. Roentgenologic examination of the skull and femur showed no abnormality but fibrosis of the lower third of the right lung.

CASE 4.—L. C., a Negress aged 13,[45] had multiple punched-out ulcers on the legs which healed at the end of nine months. Healing would occur on one side with destruction on the other. The spleen was not palpable.

Examination of the blood showed: 4,650,000 red blood cells per cubic millimeter, 80 per cent hemoglobin, 8,400 leukocytes per cubic millimeter and a color index of 0.86. The differential count showed: polymorphonuclear neutrophils 52 per cent, lymphocytes 36 per cent, monocytes 4 per cent, eosinophils 4 per cent, mast cells none and transitional cells 4 per cent. Sickle cells were looked for on nine occasions. On admission they constituted 15 to 20 per cent of the erythrocytes, but later only occasional ones were found. The reticulocytes ranged from 0.9 to 1 per cent on fourteen examinations. The Wassermann and Kline tests gave negative results, and there was no serologic response to a provocative injection of neoarsphenamine. The reaction to a tuberculin test was negative. Biopsy was not permitted.

---

45. Presented at a meeting of the Cleveland Dermatological Society on April 28, 1938 by Dr. W. F. Schwartz.[40]

CASE 5.—L. O. C., a Negress aged 14,[45] sister of the preceding patient, had multiple ulcers on the legs, which also required nine months for healing. These were punched out, with deep, sharp margins and gray, moist bases.

Examination of the blood showed: 4,950,000 red blood cells per cubic millimeter, 15,750 leukocytes per cubic millimeter and 90 per cent hemoglobin. A differential count showed: polymorphonuclear neutrophils 73 per cent, lymphocytes 15 per cent, monocytes 9 per cent, eosinophils 1 per cent and stab cells 2 per cent. The sickle cells ranged from 10 to 15 per cent on admission to 1 per cent or less on later examinations. The Wassermann reaction was negative on three occasions, and the Kline "diagnostic" test gave a negative reaction once and a 2 plus reaction twice. The reactions to tuberculin tests were negative. Biopsy was refused.

In our opinion the first 3 cases are definite instances of sickle cell anemia, the fourth probably so and the fifth possibly so, with a remission in the anemia at the time the blood was examined.

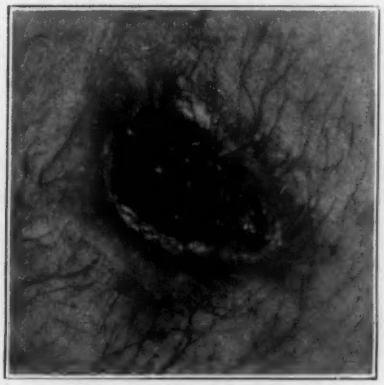


Fig. 7 (case 5).—One of the ulcers on the outer anterior surface of the right leg.

FREQUENCY OF OCCURRENCE OF ULCERS OF THE LEGS

After examining parallel series of Negroes with and without the trait, Diggs, Ahmann and Bibb[8] stated that they did not feel that their statistical results supported the idea that the ulcers on the legs occurred more commonly in those with the trait than in normal persons. In regard to sickle cell anemia, on the other hand, Diggs and Ching[3] stated that chronic ulcers or scars of old ulcers are present in 3 of every 4 adults with the disease but are infrequent in young children. They gave the average age of patients at the time of appearance of the ulcers as 15 years.

Several series of cases are on record, and from them one may obtain statistics to aid in estimating the frequency of these ulcers. In Huck's[9] series of 14 cases, there were ulcers on the legs in 2. Hein, McCalla and Thorne[25] collected 12 cases in the literature to 1927 and observed that

there were ulcers in the ankle region in 9. Corrigan and Schiller [46] observed and reported 8 cases, in which ulcers of the legs were noted in 1 and ulcers on the elbows in 2. Diggs, Pulliam and King [20] reported a series of 30 cases, in 9 of which there were ulcers on the legs. Levy [47] described 9 cases and mentioned ulcers of the legs in 1 and numerous scars in another. Anderson and Ware [48] collected from the literature 49 cases. In the 28 in which mention was made ulcers of the legs were noted in 20 and were absent in 8. In studying this report one finds that in the group of patients showing ulcers, the age of the youngest was 8 years; all the others were 15 years of age or older, while those showing no ulcers ranged from ½ year to 13 years.

DESCRIPTION OF ULCERS

In the available descriptions, one is impressed with the recurrence of the phrase "punched out." The ulcer may be single and unilateral, but multiple and bilateral ulcers are reported. The most frequent location is in the neighborhood of the ankle, but any part of the leg may be involved. The size ranges from that of a quarter or a half-dollar to much larger. It is usually sharply marginated, round or oval and may be shallow or deep. The borders may be elevated and irregular. The base usually shows granulation tissue and is occasionally suppurating or in some instances covered with dried serous or seropurulent crust. The appearance may even be that of ecthyma. The resulting scars are atrophic, glossy, smooth, depigmented and usually surrounded by a pigmented border or areola.

In their course the ulcers are typically chronic but respond to palliative and simple measures, such as elevation of the leg with rest in bed and dressings of boric acid or zinc oxide ointment. As Huck remarked, the disease itself has never been cured, but with treatment and rest the relapses are shortened and the remissions made longer. Hard physical work is detrimental.

HISTOLOGIC PICTURE

Huck's [9] description is the earliest. He observed that near the edge of the ulcer the papillae extended downward to an abnormal degree and that the connective tissue of the corium was increased above the normal amount. The walls of the rather numerous blood vessels were not abnormal. Throughout the tissues mononuclear wandering cells of the ordinary variety characteristic of chronic inflammation were scat-

46. Corrigan, J. C., and Schiller, I. W.: Sickle Cell Anemia: Report of Eight Cases, One with Necropsy, New England J. Med. **210**:410-417, 1934.

47. Levy, J.: Sicklemia, Ann. Int. Med. **3**:47-54, 1929.

48. Anderson, W. W., and Ware, R. L.: Sickle Cell Anemia, Am. J. Dis. Child. **44**:1055-1070 (Nov.) 1932.

tered diffusely, although in most places the plasma and large mononuclear wandering cell types predominated over the small lymphoid type. Among these nononuclear cells were a few neutrophilic polymorphonuclear leukocytes. In places the wandering cell infiltration was concentrated about small blood vessels and atrophic sweat glands, although many other blood vessels were entirely free from perivascular infiltration. The

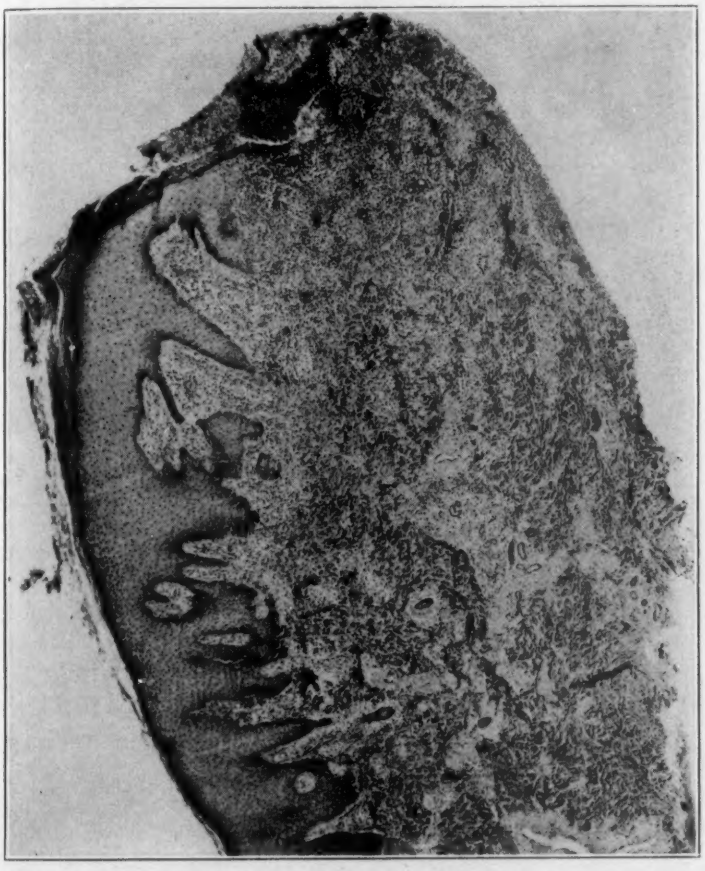


Fig. 8 (case 2).—Hyperkeratosis and acanthosis in epithelium at the edge of an ulcer, with some broadening of papillary bodies and infiltration of corium (× 35).

base of the ulcer was composed of granulation tissue possessing no characteristics suggestive of any specific causation. A few sickle-shaped red blood cells were seen.[49]

49. To demonstrate sickle cells in the tissues, most investigators insist on the desirability of using a solution of formaldehyde as fixative rather than Zenker's solution.

Sydenstricker [50] described the section in 1 of his cases as showing extreme round cell infiltration of the skin and subcutaneous tissues adjacent to the ulcer, the base being filled with granulation tissue in which there was a moderate degree of polymorphonuclear infiltration. A

Fig. 9 (case 2).—The edge of the ulcer, showing infiltration of corium with lymphoid and plasma cells to the left and the granulation tissue in the ulcer at the right (× 145).

few giant cells were seen. In the biopsies reported here no change in the tissues was noted which might not be found in any chronic, nonspecific ulcer.

50. Sydenstricker, V. P.: Further Observations on Sickle Cell Anemia, J. A. M. A. **83**:12-17 (July 5) 1924.

DIFFERENTIAL DIAGNOSIS

With ulcers of the legs in a Negro patient, the differential diagnosis may be exceedingly difficult because of the lack of a characteristic clinical or pathologic picture.

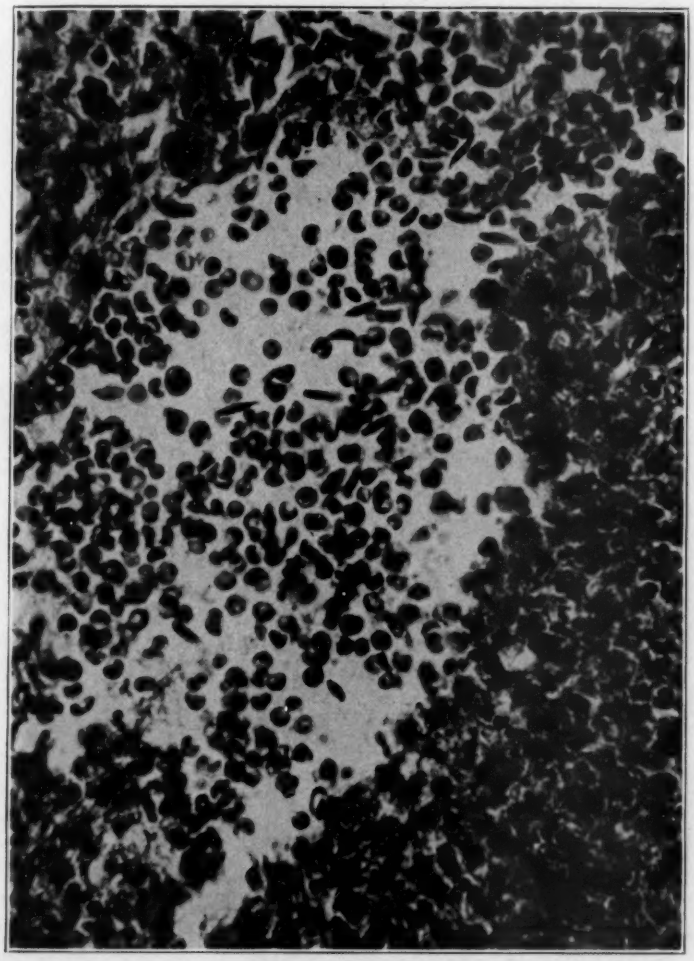


Fig. 10 (case 2).—Sickle cells in the granulation tissue in the floor of ulcer (× 605).

Merely finding sickle cell anemia in a patient with ulcers of the legs does not of itself establish a causal relation. It is impossible to reply entirely on serologic tests to differentiate between ulcers due to sickle cell anemia and those due to syphilis, for the great frequency of positive results of serodiagnostic tests in Negroes is well recognized. Antisyphi-

litic treatment aids in establishing a diagnosis, since sickle cell ulcers show no response to it. Ecthyma seldom needs serious consideration. Erythema induratum rarely if ever occurs in males; its lesions by predilection are on the calf, while those of sickle cell anemia are usually over

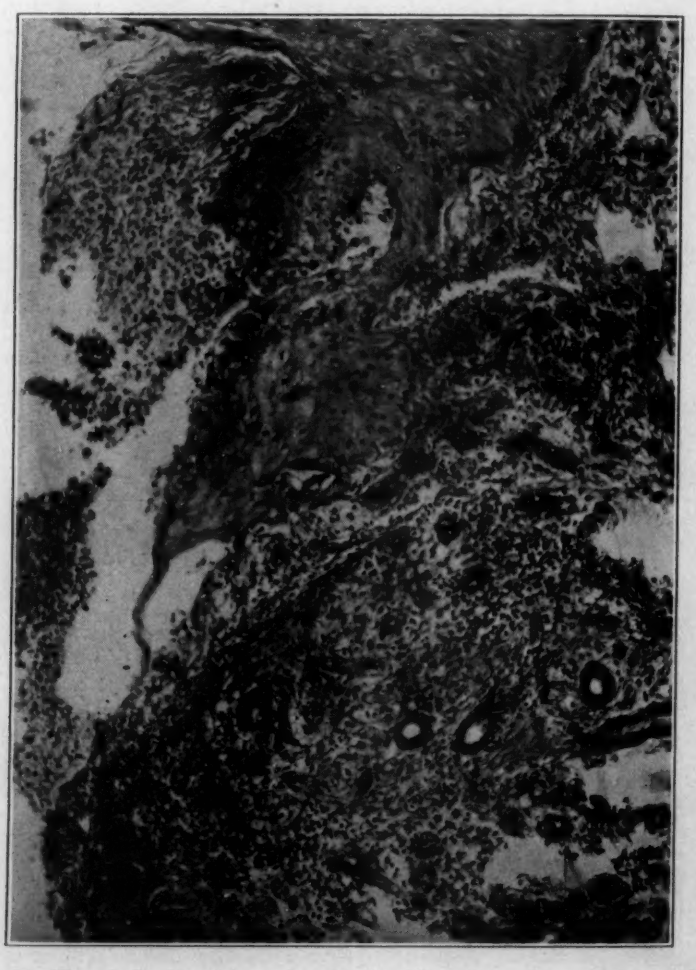


Fig. 11 (Dr. C. B. Norris' case).—At the edge of an ulcer, with granulation tissue in the ulcer and in the corium, new connective tissue, many capillaries and infiltration with round cells and occasional polymorphonuclear leukocytes (× 140).

the ankles or on the shins. Scrofuloderma occurs typically as an ulceration of the skin over tuberculous bones, joints or glands, with ragged, undermined edges and a base often covered with seropurulent exudate. With the tuberculous gumma, the history would indicate that the lesion started as a circumscribed nodular infiltration of the subcutaneous tissue,

gradually enlarging, with later involvement of the skin, and eventually breaking down to form an ulcer with a livid periphery and ragged, thin, undermined edges. A biopsy should be especially useful in establishing its tuberculous nature.

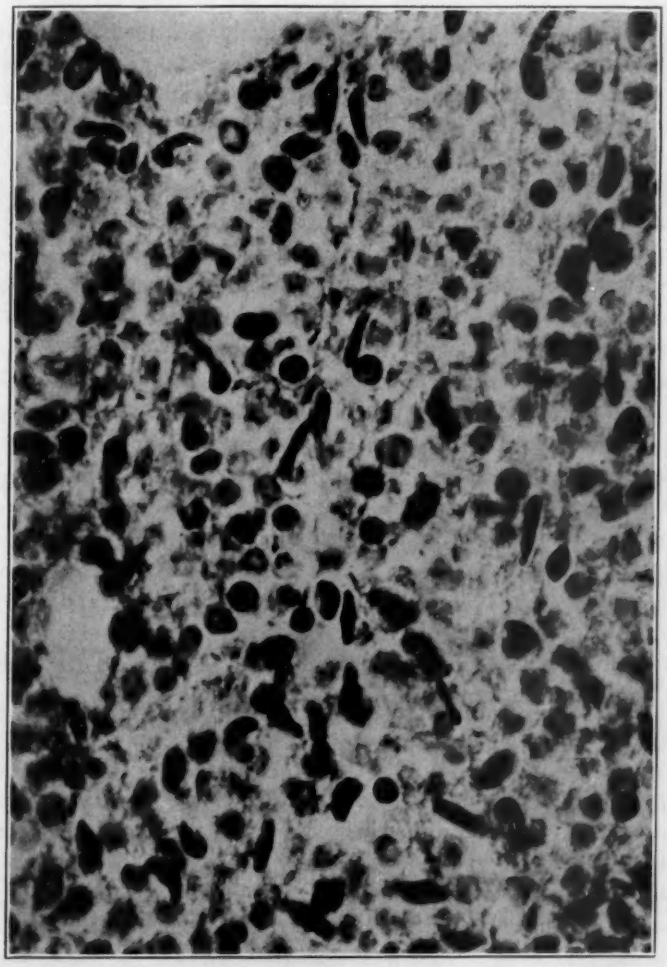


Fig. 12 (Dr. C. B. Norris' case).—Granulation tissue in the ulcer with elongated and crescentic erythrocytes (× 875).

Traumatic ulcers in the acute stage are usually inflammatory and may present evidence of surrounding cellulitis. Although some of the sickle cell ulcers apparently start from minor trauma, the purely traumatic lesion heals comparatively quickly, while in a sufferer from sickle cell anemia, trauma initiates an ulcer characterized by destruction out of proportion to the original injury and by extremely slow healing. The

chronic ulcer of the leg so frequently seen in dispensary practice in association with varicose eczema and edema of the foot and leg is rarely encountered in adolescence and, in any event, should not cause diagnostic difficulty.

ULCERS OF THE LEGS IN OTHER ANEMIAS

In considering ulcers of the legs in sickle cell anemia, the question of their occurrence in other forms of severe anemia naturally arises. Such ulcers have never been regarded as part of the clinical manifestations of pernicious anemia, although there is a recent report by Lasch [51] of a 44 year old man suffering from pernicious anemia who showed symmetric, deep, palm-sized ulcers on both legs above the ankle joints. These had not healed under treatment with salves but did with liver therapy. In an article by Chevallier [52] on dermatoses of the anemias there is no reference to ulcers on the legs. In a recent publication by Murphy [53] such ulcers are not mentioned as occurring in chlorosis.

However, with congenital hemolytic jaundice the case is different. Taylor [54] recently recounted the case of a woman 20 years old with congenital hemolytic jaundice who had an ulcer of twelve months' duration which healed promptly after splenectomy and had remained healed when last seen nine months after surgical treatment. He found reports of 17 similar cases in the literature. Since then McGovern [55] has presented at the Montreal meeting of the American Dermatological Association a white man, 23 years old, with hemolytic jaundice who had been under observation for two years for indolent multiple ulcers of both legs. Biopsy showed chronic ulcer with fibrosis at the base and recent extensive hemorrhage. Murphy [53] likewise referred to the finding of ulcers on the legs in familial hemolytic jaundice.

COMMENT

An attempt to explain the causation of ulcers of the legs in sickle cell anemia might well lead into theoretic speculation. At hand are the following facts:

1. Such ulcers occur in a definite proportion of persons suffering from sickle cell anemia and in a lower proportion of those with the sickle cell trait only.

---

51. Lasch, F.: Ueber Beingeschwüre bei pernizioser Anämie, Deutsche med. Wchnschr. **65**:377-378, 1939.

52. Chevallier, P.: Die Dermatosen der Anaemie, Med. Welt **10**:120-122, 1936.

53. Murphy, W. P.: Anemia in Practice: Pernicious Anemia, Philadelphia, W. B. Saunders Company, 1939.

54. Taylor, E. S.: Chronic Ulcer of the Leg Associated with Congenital Hemolytic Jaundice, J. A. M. A. **112**:1574-1576 (April 22) 1939.

55. McGovern, J. J.: Hemolytic Jaundice with Ulceration of the Skin, Arch. Dermat. & Syph. **41**:408-409 (Feb.) 1940.

2. They must be rare in pernicious anemia and chlorosis, at least sufficiently so that they are not generally referred to in articles on these disorders, but they are encountered in congenital hemolytic jaundice. It is possible that they occur more frequently than is recognized now.

3. Sickle cell anemia and congenital hemolytic jaundice present different hematologic pictures. In sickle cell anemia the erythrocytes frequently show elongated forms while in congenital hemolytic jaundice they are spherocytic and microcytic. In the former the fragility of the red blood cells as determined by tests with hypotonic solution of sodium chloride is decreased whereas in the latter the reverse is true. However, Murphy [53] has advanced the opinion that sickle cell anemia may be considered as the typical manifestation of familial hemolytic anemia in the Negro. It is his opinion that in place of the spherical erythrocytes characteristic of congenital hemolytic jaundice, sickle cells appear in the Negro, possibly because of some difference in the structure of the erythrocytes in Negroes as opposed to those in white persons.

4. In many case reports it is evident that the ulcers in sickle cell anemia seem to have been induced, or at least preceded, by infection or trauma. The size and duration of the ulcers are out of all proportion to the severity of the original infection or trauma.

5. The ulcers in sickle cell anemia show no specific histologic picture to distinguish them from other chronic ulcers.

With these facts at hand, the following theories may be advanced and evaluated. The first is that the ulcers have been produced by injury or infection and have become chronic simply because of associated malnutrition or the lowered vitality of anemic tissue. Against this is the present apparent lack of evidence that similar lesions occur in other severe anemias, notably chlorosis, a condition which affects adolescent girls in the same age period as those with sickle cell anemia in whom ulcers of the legs most frequently develop. That they are coincidental only is not plausible, because they occur more often in those with sickle cell anemia than in those with the nonsymptomatic trait. An explanation that the ulcers are essentially thrombotic, produced primarily by blocking of the capillaries by the greatly elongated erythrocytes, would be an attractive one but has no histologic evidence and would not explain similar ulcers in chronic hemolytic jaundice, in which thromboses are not a part of the pathologic process and in which the erythrocytes are not elongated but spherocytic.

Ultimate decision must await further and more complete clinical investigation. As Senear [56] remarked, the opportunity of studying a most interesting new condition in dermatology will be provided if anemia is considered as a possible explanation for old chronic ulcers on the legs, especially in young persons.

---

56. Senear, F. E., in discussion on McGovern.[55]

SUMMARY

The sickle cell trait is limited almost exclusively to persons of the Negro race, occurring in about 8 per cent. It is familial and apparently hereditary. There is no preference for sex and no difference in percentage incidence in different sections of the country. Anemia, which is found only in some of those who show sickle cells in the peripheral blood, may be accompanied by some or all of a group of signs and symptoms, which includes ulcers on the legs.

Histories of illustrative cases in which ulcers occurred on the legs have been recounted. It is impossible to state definitely the frequency of occurrence of ulcers or scars of ulcers, because of the insufficiency of statistical data, but in the largest series of collected cases, numbering 28, ulcers or scars were noted in 20.

The ulcers are usually punched out in appearance, may be single or multiple and unilateral or bilateral and are most frequently in the neighborhood of the ankle. The course is extremely chronic. Simple local applications seem the most effective treatment. No treatment is known for the underlying anemia.

The histologic picture is that of chronic granulomatous ulcer.

Diagnosis rests on: the finding of a hemolytic type of anemia with sickle cells in the peripheral blood, chronicity, the absence of specific architecture in the histologic examination of biopsy material and the failure to respond to antisyphilitic treatment when the results of serodiagnostic tests for syphilis are positive.

The mechanism of the causation of the ulcers on the legs is an open question. Undeniably many seem to have been initiated by minor infection or trauma. That they are also seen in congenital hemolytic jaundice is of interest and suggests that a common causative factor may be found.

In dermatologic practice anemia should be considered as a possible explanation for old chronic ulcers on the legs, especially in younger persons.

Dr. Harold N. Cole and Dr. J. R. Driver gave permission to refer to the histories of cases 2, 4 and 5, observed in their service at the Cleveland City Hospital as well as in our own service. Dr. Gerard DeOreo assisted in collecting data and photographs. Prof. Howard T. Karsner made photomicrographs at the Institute of Pathology of Western Reserve University. Dr. Louis W. Ladd Jr. and Dr. M. I. Sparks made the hematologic studies in 2 cases. Dr. Fred C. Oldenburg gave permission to report cases observed in the medical service of St. Vincent Charity Hospital.

The photomicrographs in figures 11 and 12 are from the case reported by Netherton.[38] Dr. Claude B. Norris, who saw the patient originally, procured the slide for us.

1010 Hanna Building, 1422 Euclid Avenue.

669 Rose Building, 20 East Ninth Street.

ABSTRACT OF DISCUSSION

DR. E. W. NETHERTON, Cleveland: This excellent presentation by Dr. Cummer and Dr. LaRocco is a timely one. Although in the first case, which was reported by Herrick, there were ulcers of the legs, there is only one article in the dermatologic literature in this country which places any emphasis whatever on this entity.

It is well known that sickle cell anemia is almost always observed in Negroes, although there have been a few apparently bona fide cases reported in white persons. In some of those cases, however, it has not been possible to rule out with certainty the possibility of Negro blood. The sickling trait has a higher incidence among Negroes. Although 8 per cent of the Negroes show this trait, a much smaller per cent show the anemia. Only in a case in which the anemia develops is one apt to see this particular type of ulceration. The spleen in sickle cell anemia is invariably large early in the disease, while late in the disease it is apt to be small, often impossible to be detected when splenectomy is attempted in the treatment of this disease. Repeated infarcts and subsequent sclerosis lead to atrophy of the spleen. I mention that because it may at least be of some theoretic importance regarding the pathogenesis of these ulcers.

Dr. Cummer mentioned that there is no explanation for the mechanism producing these ulcers, but all the histologic studies have been made on late lesions, in which the early initial change has been cast off as the ulcer formed. As he has emphasized, the theory of trauma plus secondary infection will not explain the mechanism. Formation of ulcers in this way obviously occurs in all anemias. However, only in this particular anemia is this type of ulcer found. Therefore, I believe that if some one could obtain the tissue from a very early lesion, which is not easily done, and make serial sections, he might find certain vascular changes, such as thrombi, in the early tissue changes similar to those frequently occurring in the spleen.

I think that if more careful search is made for cases of this kind, it will be found that they are more common than was believed.

DR. MARTIN T. VAN STUDDIFORD, New Orleans: Dr. Cummer, in his paper, has introduced the discussion of a condition which is known to exist but which is seldom seen. When ulcers of the legs are shown to medical students, they proffer a diagnosis of "sickle cell anemia ulcer," whereas the condition is usually a syphilitic or a varicose ulcer.

Of the many cases of sickle cell anemia observed in St. Vincent Charity Hospital over twenty years, I have just lately had a patient, a Negro boy 4 years old, who has ulcers over traumatic areas from his waist to his ankles. He has a total erythyrocyte count of 200,000 per cubic millimeter and has received five transfusions. A doughy "pot belly" is developing, and he is becoming emaciated over the chest and shoulders.

DR. CLYDE L. CUMMER, Cleveland: Haden and Evans studied the literature, carefully analyzed all the cases presumably reported in white persons and concluded that after any possibility of a trace of Negro blood had been ruled out—of course, that is difficult to do—there were 8 authentic examples of the condition in white persons, practically all in Italians or in persons of Mediterranean stock.

It is interesting, with that in mind, that there is a similar type of anemia, so-called Cooley's erythroblastic anemia or the Mediterranean anemia, which occurs in persons of Mediterranean stock (Wintrobe, M. M.; Matthews, E.; Pollack, R., and Dobyns, B. M.: Familial Hemopoietic Disorder in Italian Adolescents and Adults Resembling Mediterranean Disease [Thalassemia], *J. A. M. A.* **114**:1530 [April 20] 1940).

MASSIVE DESTRUCTION OF THE FACE

CHARLES C. DENNIE, M.D.
Professor of Dermatology

THOMAS R. HAMILTON, M.D.
Assistant in Pathology

AND

HENRY F. QUINN, M.D.
Resident in Dermatology

KANSAS CITY, KAN.

Massive destruction of the face is rather a rare condition. A diversity of etiologic factors have been given credit for its production. Among the principal causes of the condition are syphilis, frambesia, extensive rodent ulcer, tuberculosis, leishmaniasis (American), leprosy and gangosa (probably a tertiary form of frambesia).

The two main possibilities to be considered in the case to be reported are syphilis and American leishmaniasis. In America it is hard to prove that a case is one of leishmaniasis. It may have all of the typical findings, and yet the etiologic factor cannot be demonstrated. We observed such a case in the Kansas City General Hospital for nine months, in consultation with Dr. Paul F. Stookey.

The patient was a Central American who came to the hospital because of a perforation in the septum of his nose and a fissure at the junction of the left nostril and the lip. All serologic reactions were negative, and there was no history of syphilis. The disease progressed until the patient before death had lost not only his nose but his upper jaw, malar bones, eyes and lower jaw. Histologic examination of the tissues showed no leishmanias. Inoculation of diseased material into guinea pigs gave negative results. A section of the tissue was sent to Montenegro in Rio de Janeiro, Brazil. He was unable to demonstrate such bodies. A complete autopsy revealed no significant changes and no confirmatory evidence of leishmania infection.

According to Wilson and others, American leishmaniasis does not attack the viscera or the lungs. On the other hand, physicians of South America, where the disease is prevalent, in personal conversation told one of us (C. C. D.) that in American leishmaniasis the viscera are often involved.

From the University of Kansas School of Medicine.

Read at the Sixty-Third Annual Meeting of the American Dermatological Association, Inc., Colorado Springs, Colo.

REPORT OF A CASE

History.—A man aged 38, a native Kansan, who had never been outside of the United States, was admitted to the hospital in February 1938, complaining of a discharge from his nose. There was an indefinite history of syphilis nine years before his entry into the hospital. He stated that a white spot had developed in the roof of his mouth, which disappeared when he was given several injections in the arm and in the hip.

When the patient was first admitted to the hospital, a diagnosis was made of chronic ethmoid sinusitis and infection of both antrums. The treatment at that time consisted of the exploration of the left frontal sinus and right antrotomy. The serologic reactions for syphilis were negative.

He was admitted again on July 27, 1938, at which time a diagnosis was made of perforation of the septum due to syphilis. He remained only a few days and was discharged from the hospital. He was readmitted in November, at which time we saw him.

Physical Examination.—The patient was rather poorly nourished but fairly well developed and not acutely ill and had a red, swollen, shiny nose, with a rounded tumor on each side involving the tear duct (bilateral dacrocystitis). There was an offensive discharge from the nose. The nasal septum showed a perforation more than 2 cm. in diameter. The entire nose was tender and greatly enlarged, so that it drifted down toward the corner of the mouth. There were no abnormalities in the throat, but an examination of the neck showed some enlargement of the lymph nodes at the angle of the jaw. The chest was normal, and no abnormalities of the heart were discovered. An examination of the abdomen revealed no palpable organs or masses. The reflexes were physiologic. The extremities were normal. The nose, which at first showed no ulceration on the outside, became necrotic on the left side. It became plastic and drifted down over the upper lip. The process continued until the nose was entirely destroyed. Accompanying this destruction, the walls of the sinuses disappeared, the upper jaw disappeared, except for a thin strip of bone, the sphenoid sinus was exposed, and both eyes became involved, with final total blindness. A huge opening was made in the face, of such magnitude that the convulsive action of the esophagus could be clearly seen.

Laboratory Tests.—Serologic reactions for syphilis of both the blood and the cerebrospinal fluid were negative. There were moderate anemia and a moderate increase in leukocytes. A dark field examination of the material draining from the nose showed the presence of numerous spirochetes, which were of two types: the large, coarse spirals of Vincent, together with fusiform bacilli, and smaller, motile spirochetes morphologically identical with Spirochaeta pallida. It was considered at this time that the patient had syphilis but was suffering from a negative phase of it; in other words, his immunologic forces were so low that he had no resistance to his syphilis. He was given potassium iodide and intramuscular injections of a bismuth compound, with no benefit. Hyperpyrexia by means of hot baths was then instituted. After administering ten baths, in which the temperature was raised to 105 F., without improvement, the treatment was changed to the intravenous administration of typhoid bacterin. After a large number of successful elevations in temperature, this method was discontinued as the disease was progressing rapidly. By this time he had lost the left side of his nose and had so much necrotic material in his face that a surgical operation was performed to remove the material. Several doses of mapharsen were given,

without result. The two types of spirochetes could still be demonstrated in the secretions from his nose. He died on Aug. 18, 1939.

Autopsy.—The anatomic diagnoses were ulcerating phagedenic granuloma of the face and frontal portions of the skull; extensive necrotizing cellulitis of the face and head; chronic abscess of the brain (right frontal lobe); localized chronic pachymeningitis; bilateral confluent bronchopneumonia with early abscess formation (right lung); acute fibrinous pleurisy; acute dilatation of the heart; parenchymatous degeneration of the liver and kidney, and acute and chronic splenitis.

Histologic Examination.—Sections of material from several places in the active lesions about the face were made. The stratified squamous epithelium was irregularly thickened and ulcerated at a number of points. In some areas the superficial squamous cells showed extensive vacuolation. The underlying hyaline fibrous

Fig. 1.—Massive destruction of the face.

connective tissue showed a few, diffusely scattered mononuclear leukocytes. In other places there was a distinct mononuclear perivascular infiltration, with an increase in blood vessels to such an extent that it had the appearance of an angioma. There were no carcinomatous cells demonstrated. Sections taken from the diseased areas of the face were impregnated by the Levaditi method, and numerous spirochetes of two varieties were demonstrated: the large, coarse spirals belonging to the Vincent group and the smaller, sharply turned spirals, morphologically similar to S. pallidae. On numerous occasions these same organisms had been demonstrated by dark field illumination and by Fontana's stain. These organisms did not disappear on the administration of mapharsen. They were present in the tissue until the patient's death.

Liver: The liver was lobulated. The capsule was irregularly thickened. A few clumps of red blood cells were adherent to the surface. A few patches of liver cells were seen showing rather marked vacuolation. In other areas the liver cells were irregularly swollen and the sinusoids were compressed. There was considerable congestion, particularly in the central zone throughout the organ.

The portal spaces showed moderate mononuclear infiltration. Some of the blood vessels contained masses of agglutinated red cells, together with fibrin and a few leukocytes.

Spleen: The capsule of the spleen was not thickened. The trabeculae were not unduly prominent. The malpighian bodies were rather numerous and well defined. The sinusoids throughout the pulp were prominent, and there was diffuse

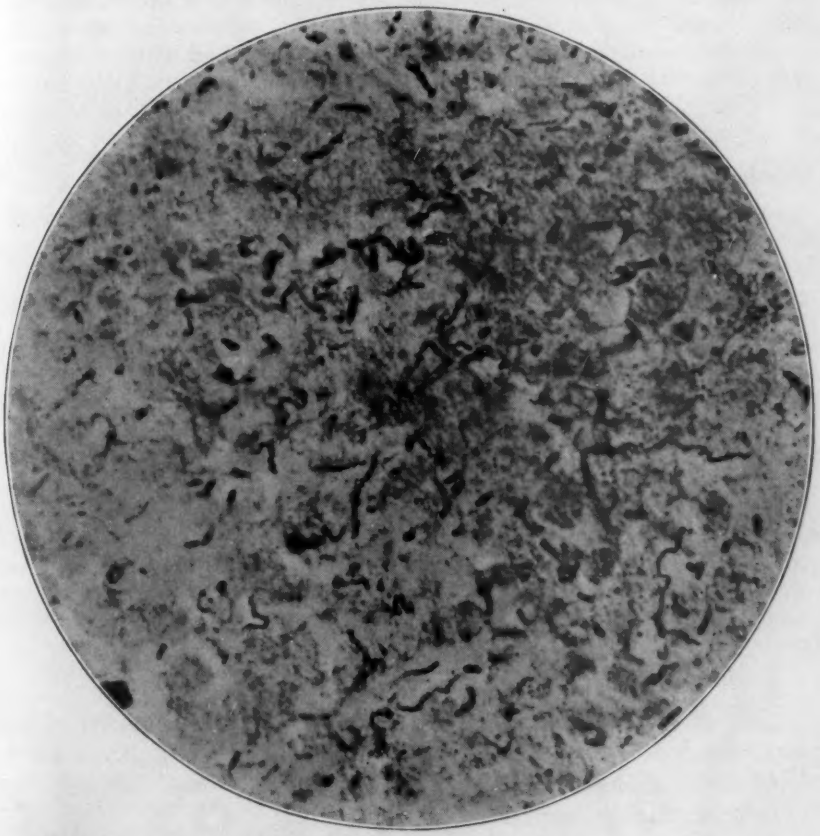


Fig. 2.—Photomicrograph of a section of tissue taken from the advancing border of a gigantic ulcer of the face, showing S. microdentium and some of the larger spirals belonging to the Vincent group.

fibrosis. Polymorphonuclear leukocytes were scattered throughout the pulp, and the sinusoids were considerably congested.

Brain: The thickened dura was adherent to the arachnoid on the right anterior lobe of the cerebral hemisphere. This area was contiguous to the diseased portion of the skull. Marked pachymeningitis was present. Beyond this was a small abscess, extending 1.5 cm. into the brain substance. The abscess was surrounded by a dense yellowish gray fibrous material. The histologic picture was that of chronic granuloma.

Animal Experimentation.—Several months before the patient died, material was removed from the face and injected into the testes of two rabbits. At the end of three days a distinct chancre developed in one rabbit, which cleared up in about ten days. In the other rabbit a chancre developed in three weeks, from which both types of spirochetes, already described, were recovered on dark field illumination, by Fontana's stain and by Levaditi's impregnation method. In the rabbit in which the successful inoculation was secured a sloughing, gangrenous ulcer developed, which extended to and through the inguinal region and produced the rabbit's death. An inoculation from this rabbit to a tandem rabbit produced a chancre-like lesion, but unfortunately the rabbit died before we were able to complete our work.

COMMENT

We were unable to demonstrate Leishmanias in any of the tissues, although a more complete examination is yet to be made.

We do not believe that the spirochetes that were demonstrated were S. pallida, in spite of the fact that they were morphologically identical with it. The coarse spirals undoubtedly belong to the Vincent group. We are of the opinion that the small spirals belong to the microdentium family. Spirochaeta microdentium is a normal inhabitant of the mouth. It is considered to be nonpathogenic, yet we have encountered cases of partial destruction of the jaw in which the only organisms found were of this species. We believe that these organisms are capable of becoming pathogenic in persons who are in an anergic state. The massive destruction of the face can be produced by these spirochetes, similar to the condition produced in the cheeks of children known as noma or cancrum oris. One of us (C. C. D.) demonstrated such spirochetes in the gangrenous tissue of an infant's cheek. The primary seat of attack was the nasal septum. The tear ducts were secondarily involved.

SUMMARY

We present a case in which we believe Spirochaeta microdentium was responsible for the massive destruction of the face, although it is hard to prove this assertion. We have not eliminated the possibility of American leishmaniasis.

1524 Professional Building.

ABSTRACT OF DISCUSSION

Dr. A. Benson Cannon, New York: In the past several years a number of cases similar to the one presented here have been observed. In almost every instance the diagnosis was one of a variety of conditions: syphilis, tuberculosis, carcinoma or noma. The destructive process usually appeared after an operation, such as an appendectomy, or after ineffective treatment of a local injury or of a disease, such as syphilis or an abscess.

I recall that a number of years ago I was called in consultation with the late Dr. George E. Brewer on a case of massive destruction of the abdominal wall, which had occurred after the removal of an apparently innocent appendix.

Around the stitch wound there appeared ulcerations, which spread rapidly over the skin and soft parts, extending down to the fascia and involving the entire abdominal wall. The patient died, as did 3 or 4 others with similar conditions whom I have seen since.

In 1926 Dr. Frank Meleney, who made extensive bacteriologic investigations in several cases of the same condition, reported with Dr. Brewer (*Ann Surg.* **84**:438 [Sept.] 1926) that they had been able to isolate from the wounds of these patients an anaerobic, microaerophilic, nonhemolytic strain of Streptococcus and also a hemolytic strain of Staphylococcus aureus, and that they considered the ulcerations to be due to the symbiotic action of the two micro-organisms. Brewer and Meleney treated the wounds with hydrogen peroxide and then packed them with gauze wet with solution of formaldehyde for two days, after which they applied the Carrel-Dakin treatment (with dilute solution of sodium hypochlorite). The improvement was immediate and progressive, the wounds healing rapidly and the patients all recovering within a few weeks or months.

Recently at the Vanderbilt Clinic I encountered a similar case in which after surgical removal of an axillary gland the entire axilla and the greater part of the skin and subcutaneous tissue of the chest wall on the side operated on sloughed away. This patient was presented at a local meeting of dermatologists, who were about equally divided in their opinion as to whether the condition was tuberculosis or syphilis. After about eleven months of treatment for the two diseases the patient was admitted to the Presbyterian Hospital, where he was studied and treated by Dr. Meleney in the manner used by Brewer and Meleney in the cases to which I referred, and was discharged as cured a few months later.

At a recent meeting of the New York Academy of Medicine a syphilitic patient from the Vanderbilt Clinic was shown in whom the nose as well as the adjacent portions of the cheek and lip had sloughed away, in spite of the fact that he was receiving active antisyphilitic therapy (old arsphenamine, a bismuth preparation and iodides). The spreading of the ulcerative process was checked only after vigorous local antiseptic treatment of the type advocated by Brewer and Meleney.

I could enumerate a number of additional interesting cases of similar nature in which the condition has responded to this treatment when all other remedies had failed.

I do not believe that the dermatologists in general have been as quick to recognize the value of the antiseptic method of treatment as have the surgeons, by whom it was so carefully and thoroughly worked out in the first place. I feel strongly that in cases of destructive processes of the type presented here one should not overlook the therapeutic possibilities inherent in the Carrel-Dakin method of treatment.

Dr. Charles C. Dennie, Kansas City, Kan.: I neglected to state that there were certain areas in the face in which there were large collections of small blood vessels. The pathologist was inclined to make a diagnosis of angioma.

Aseptic dressings were used, and the dead tissue was removed wherever possible.

I believe, in agreement with Dr. Wile, that the process in this case was one of endarteritis, continuous, with necrosis, due to S. microdentium.

ACETYLGLYCARSENOBENZENE IN TREATMENT OF SYPHILIS

PRELIMINARY REPORT

WILLIAM H. GUY, M.D.

BERNHARD A. GOLDMANN, M.D.

GEORGE P. GANNON, M.D.

AND

JACOB SLONE, M.D.

PITTSBURGH

Since Ehrlich's discovery of arsphenamine did not accomplish the desired millennium in the treatment of syphilis, scientific workers have been constantly seeking to improve the known methods of attack on this disease. These endeavors have been directed toward better management of the courses of treatment, modifications in the dosage of drugs, variations in the methods of administration and the addition of new chemical compounds. During the past two years we have conducted a clinical study with a new drug in 84 cases of various types of syphilis. An arsenical compound having the common name of acetylglycarsenobenzene was administered intramuscularly, together with an oil-soluble bismuth compound and insoluble mercury. The patients were a selected group who had not received previous antisyphilitic treatment. In each instance the diagnosis of syphilis was supported by a dark field examination or by a serologic test.

CHEMISTRY

Acetylglycarsenobenzene is chemically 3,4′-diacetylamino-4-hydroxyarsenobenzene 2′-sodium glycolate. The molecular weight is 530. The arsenic content is 28.3 per cent. The formula may be expressed as $C_{18}H_{17}O_6N_2As_2Na$ and graphically as:

From the Department of Dermatology and Syphilology, University of Pittsburgh School of Medicine.

Read before the Section on Dermatology at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

The drug was available in a sterile aqueous solution with 10 per cent glycerin plus 0.005 Gm. per cubic centimeter of ascorbic acid. Each cubic centimeter of the sterile solution contains 0.07 Gm. of the active constituent; in arsenic content (0.02 Gm.) this is approximately equivalent to 0.1 Gm. of neoarsphenamine. The solution in ampules is orange-yellow and neutral or faintly acid in reaction.

Local Tolerance.[1]—The local effects of acetylglycarsenobenzene were studied after subcutaneous as well as intramuscular injections of 0.1 to 0.2 cc. into adult albino rats. Groups of 12 animals were killed one, three and six days after treatment, and the sites of injection were examined. The subcutaneous and intramuscular injections produced a slight edema and congestion at the twenty-fourth hour, but little or no remarkable effect was demonstrable either three or six days after injection. Intramuscular (gluteal) injections into the upper and outer third of the buttock of man were tolerated satisfactorily, with no symptoms other than those of pressure, for from three to twenty minutes after injection.

Systemic Tolerance.—Studies of the toxicity of acetylglycarsenobenzene were made by intravenous injection into the albino rat, according to specifications of the National Institute of Health. These indicated satisfactory tolerance of not less than 400 mg. per kilogram of body weight given intravenously. When the drug was given intramuscularly the corresponding tolerated dose was 500 mg. per kilogram of body weight. (The National Institute of Health standard of tolerance for neoarsphenamine injected intravenously in the rat is 240 mg. per kilogram.)

Therapeutic Index.—In experimental infection with Trypanosoma equiperdum in rats, the curative dose of acetylglycarsenobenzene was found to be 12 mg. per kilogram intravenously. The therapeutic index (or maximum tolerated dose divided by the curative dose) thus exceeds 30.

Excretion.—The excretion curve was studied in a series of 6 adult rats after the intramuscular injection of acetylglycarsenobenzene in a dose of 50 mg. (14.28 mg. of arsenic) per kilogram of body weight. The peak of urinary excretion was observed during the first twenty-four hours; the values decreased during the following six to eight days, but a trace was still being excreted on the thirtieth day. The peak of fecal excretion occurred on the third to fourth day, and only traces were present on the eleventh day. A total of 58.5 per cent of the administered dose was recovered during the twenty-one days of study, which had

1. Data on local tolerance, systemic tolerance, therapeutic index and excretion are based on experiments by O. W. Barlow, Ph.D., M.D., Director of Pharmacologic and Biologic Research, Winthrop Chemical Co., Inc.

increased to 60 per cent on the thirtieth day. For purposes of comparison, neoarsphenamine was injected intravenously in a series of 6 cats in a dose of 50 mg. per kilogram of body weight. During the succeeding twenty-one days, 38.75 per cent of the administered dose was recovered from the urine and feces. The data indicate that the ratio of the urinary excretion to the fecal excretion of arsenic after intramuscular injection of acetylglycarsenobenzene exceeds that after intravenous injections of neoarsphenamine.

In dogs the peak of urinary excretion of arsenic following the intramuscular injection of 350 mg. per kilogram of body weight of acetylglycarsenobenzene occurred on the second day. A total of 67 per cent of the administered dose was recovered from the urine and feces during twenty-one days.

In human beings the excretion of arsenic following the injection of arsphenamine in terms of the administered dose was from 0.9 to 2.5 per cent on the first day, from 3 to 8.8 per cent in three days and from 4.9 to 13.5 per cent in fourteen days.

Weiss and Raiziss [2] reported 2.2 per cent excretion of neoarsphenamine during the first twenty-four hours. Corresponding observations on 3 normal men who received at three day intervals two intramuscular injections of 175 mg. each of acetylglycarsenobenzene gave the following excretion data: 21.5 per cent on the first day, 31.7 per cent in three days and 34.8 per cent in fourteen days.

REVIEW OF THE LITERATURE

A review of the literature discloses a number of European publications on the clinical use of acetylglycarsenobenzene (under the trade name "solusalvarsan") since 1932. These publications in the main attribute to the drug a clinical efficacy comparable to that of other arsenicals. Unfortunately, a number of these earlier reports are based on relatively short clinical studies which do not permit accurate deductions. We believe that at least two years' study is necessary for a preliminary evaluation of any antisyphilitic drug.

In 1932 Bezecny [3] presented the first publication on the clinical investigation of acetylglycarsenobenzene. From his experiences he concluded that the drug is an effective antisyphilitic preparation and that intramuscular injections in amount large enough to produce a therapeutic action could be administered without pain.

---

2. Weiss, C., and Raiziss, G. W.: Elimination of Arsenic in Urine of Syphilitic Patients After Intravenous Injection of Arsenic, Arch. Int. Med. **30**:85 (July) 1922.

3. Bezecny, R.: Dermat. Wchnschr. **94**:611 (April 30) 1932.

Ensbruner [4] summarized his study by stating that in respect to spirocheticidal properties, influence on syphilitic lesions and tolerance the drug is an effective preparation.

Sainz de Aja and Forns Contera [5] found the drug to be superior to other arsenical preparations administered intramuscularly and to be well tolerated.

Van Putte [6] remarked that acetylglycarsenobenzene is better tolerated than neoarsphenamine.

Wendt [7] concluded after a three years' study in the treatment of early syphilis that this drug is the drug of choice in cases in which intravenous injections are to be avoided. In a rather extensive series he observed no side effects.

Scherber [8] recommended its use in patients with "poor veins" and in those who react to injections of neoarsphenamine, and it was his opinion that it can replace the latter.

A number of side effects have been reported abroad, but our experience indicates that these reactions were often due to improper dosage, either an excess of drug or inordinate frequency of administration.

Fasal and Konrad [9] reported fatal complications following the intramuscular injection of the drug in 2 patients.

Grieco [10] reported a case of vesicular edematous erythroderma.

Wendlberger and Hrad [11] stated that the sole advantage of the drug would seem to be the fact that it is available in stable form, but owing to the complications of dermatitis, they recommended its use intravenously whenever feasible.

Harrison [12] considered the therapeutic action to be weaker than that of neoarsphenamine and the toxicity greater, particularly with respect to dermatitis, and did not advocate its use in the treatment of syphilis.

CLINICAL STUDY

Our investigation of acetylglycarsenobenzene has extended from March 1938 to April 1940. During this time 84 patients were given twenty-one hundred intramuscular injections of the drug. In addition

4. Ensbruner, G.: Dermat. Ztschr. **65**:28 (Nov.) 1932.
5. Sainz de Aja, E. A., and Forns Contera, M.: Actas dermo-sif. **25**:103 (Nov.) 1932.
6. van Putte, P. J.: Nederl. tijdschr. v. geneesk. **79**:3031 (June 22) 1935.
7. Wendt, H.: München. med. Wchnschr. **85**:367 (March 11) 1938.
8. Scherber, G.: Wien. med. Wchnschr. **82**:841 (June 25) 1932.
9. Fasal, P., and Konrad, J.: Med. Klin. **33**:1360 (Oct. 8) 1937.
10. Grieco, V.: Rev. Assoc. paulista de med. **9**:63 (July) 1936.
11. Wendlberger, J., and Hrad, O.: Dermat. Wchnschr. **108**:125 (Feb. 4) 1939.
12. Harrison, L. W.: Brit. J. Ven. Dis. **15**:203 (July) 1939.

to this number, 49 patients were dropped from the series because of irregularity in attendance, and the results observed in them are not included in this study.

An untreated group of patients with primary lesions, for whom a diagnosis of syphilis was established by dark field examination, received one intramuscular injection of acetylglycarsenobenzene and were immediately hospitalized to determine the effect of the drug on the disappearance of Spirochaeta pallida from the lesions. All other patients, also previously untreated, were ambulatory ones. In all cases general medical examinations were made, special attention being given to the eyes and to the cardiovascular and nervous systems.

Kahn tests were made on each patient at least once a month in the laboratory of the Falk Clinic of the University of Pittsburgh. The results obtained from this laboratory were checked with those recorded on the same blood specimen at two other laboratories, and there was little or no discrepancy in the comparative laboratory findings. The spinal fluid was checked for all patients except those who refused examination.

Of the total number of patients we are reporting on, 7 (8.2 per cent) have completed two years' treatment; 44 (52.4 per cent), eighteen months' treatment; 20 (23.4 per cent), twelve months' treatment and 14 (16.0 per cent), six months' treatment. When these were admitted to the hospital, in 48 the condition was latent, in 24 secondary and in 12 primary. We reiterate that none of the group had received antisyphilitic treatment at any previous time.

The following routine course was used in all cases, regardless of the stage of syphilis: A dose of acetylglycarsenobenzene (6 cc. for male and 4 cc. for female patients) was given once weekly for six weeks, followed by one dose (60 mg. of bismuth) weekly of an oil-soluble bismuth compound for six weeks and one dose weekly of mercuric salicylate (0.065 mg. of mercury) for six weeks.

The acetylglycarsenobenzene was administered intramuscularly, deep into the upper and outer quadrant of the gluteus maximus. There were no complaints of pain or tissue damage in patients treated in our clinic; in fact, because of this, the patients preferred injections of acetylglycarsenobenzene to those of bismuth or mercury. All patients with late stages of syphilis received supplementary medication with saturated solution of potassium iodide by mouth. Treatment was continuous, without any intervals or rest periods.

BY-EFFECTS

After the intramuscular administration of acetylglycarsenobenzene, immediate reactions, such as nitritoid crises, nausea, gastrointestinal symptoms, abdominal pain, headache, weakness and collapse, were not

observed. Herxheimer reactions occurred only in cases of early secondary or late primary syphilis, but, as a rule, these reactions were mild and not accompanied by the customary nausea or fever, being characterized by overaccentuation of the lesions. In our early experience with acetylglycarsenobenzene we gave biweekly injections of full doses. We observed dermatitis in 8 persons, progressing to the exfoliative stage in 6. This led us to the conclusion that such frequent administration of this arsenical, even in smaller doses, is contraindicated. Subsequently, our technic of administration was modified, and only one injection per week was given, the dose never exceeding 6 cc. in seven days. After this change, several persons who previously exhibited dermatitis received small doses once a week without apparent by-effect and later tolerated the full therapeutic dose. However, in 2 of these cases the dermatitis occurred after use of the modified technic.

In several of the patients in whom dermatitis developed in the early period, patch tests with arsphenamine, neoarsphenamine and mapharsen produced positive reactions. Delayed reactions, such as encephalitis, changes in the optic nerve and renal, neuritic, purpuric or hemorrhagic encephalitis, were not observed. In no patients were there recurrences of lesions on the skin or mucous membranes after medication with acetylglycarsenobenzene.

The question of depression of the hemopoietic system was given appropriate consideration. Complete studies of the blood were made on patients who had been under treatment for at least six months. In several we demonstrated minor suppression of leukocytes, with diminution in the granular elements and platelets. However, in none of these did we see the concomitant symptoms associated with granulocytopenia, and treatment was continued without further clinical developments.

Routine urinalyses were made in all cases prior to each injection of acetylglycarsenobenzene or a bismuth or mercury compound. At no time was treatment discontinued because of abnormal urinary findings.

Of the 84 patients on whom this report is based, 9 showed toxic manifestations. In 6 cases we had to discontinue the administration of acetylglycarsenobenzene because of intolerance to the drug.

One man after four doses had mild transient jaundice, which disappeared on discontinuance of administration of the drug. Subsequent treatment with acetylglycarsenobenzene was tolerated without by-effect.

EFFECT ON ACTIVE LESIONS

Primary Lesions.—After a diagnosis of syphilis had been established through dark field examination, a group of patients presenting typical primary lesions were hospitalized. Immediately on demonstration of S. pallida in the lesion, the patient was given one intramuscular injection

of 6 cc. of acetylglycarsenobenzene. Dark field examinations were repeated at intervals until three negative results were obtained. Prior to each examination of material from the lesion, the deep surrounding tissues were compressed by firm pressure in an endeavor to bring

TABLE 1.—*Results of Dark Field Examination of Patients with Primary Lesions Before and After the Administration of Acetylglycarsenobenzene and Hospitalization*

Patient	Time	Results of Dark Field Examination	Comments
B. S. Negro	9 a. m.	Positive	Drug administered
	2 p. m.	Positive	
	6 p. m.	Positive	
	9 a. m.	Negative	
	1 p. m.	Negative	
	6 p. m.	Negative	Discharged
J. T. White man	9 a. m.	Positive	Drug administered
	7 p. m.	Positive	
	9:30 a. m.	Negative	
	1:30 p. m.	Negative	
	6 p. m.	Negative	Discharged
A. J. White man	9 a. m.	Positive	Drug administered
	2:30 p. m.	Positive	
	6 p. m.	Positive	
	8:30 a. m.	Few nonmotile organisms	
	1 p. m.	Negative	
	6 p. m.	Negative	
F. L. Negro	9 a. m.	Positive	Drug administered
	6 p. m.	Positive, poor motility	
	9 a. m.	Positive, no motility	
	1 p. m.	1 organism seen, no motility	
	6 p. m.	Negative	
	9 a. m.	Negative	
	1 p. m.	Negative	Discharged
L. S. Negro	9 a. m.	Positive	Drug administered
	5:30 p. m.	Negative	
	9 p. m.	Negative	Discharged
R. R. White man	9 a. m.	Positive	Drug administered
	6 p. m.	Negative	
	8 a. m.	Negative	
D. G. White man	9 a. m.	Positive	Drug administered
	2:30 p. m.	Positive	
	6 p. m.	Positive	
	9:30 p. m.	Positive	
	11 a. m.	Negative	
	4 p. m.	Negative	
	9 p. m.	Negative	Discharged

spirochetes to the surface. A résumé of our dark field findings in this group is given in table 1.

Secondary Lesions.—One case of secondary syphilis presenting condylomas in which active spirochetes were demonstrated was included in this study (table 2).

It will be noted that in the 7 cases of primary lesions negative results of dark field examinations were obtained within the following time

intervals: in 1 case ten hours, in 1 eighteen hours, in 3 twenty-four hours, in 1 twenty-six hours and in 1 thirty hours. It is evident that in primary lesions the drug has a rapid destructive effect on the spirochetes, for in most instances the result was negative within twenty-four hours. Apparently, therefore, the action of the drug on primary lesions is comparable to that of arsphenamine, neoarsphenamine or mapharsen. Continuous observation of these patients demonstrated that there was no recurrence of cutaneous manifestations but that with continued treatment there was rapid retrogression of the lesions.

In patients with primary syphilis the following results of treatment on the serologic reactions and on disappearance of lesions were obtained: The lesion disappeared in an average time of nineteen and five-tenths days, or after an average of five and two-tenths injections totaling

TABLE 2.—*Results of Dark Field Examination of a Patient with Secondary Syphilis Before and After the Administration of Acetylglycarsenobenzene and Hospitalization*

Patient	Time	Results of Dark Field Examination	Comments
J. W.	9 a. m.	Positive	Drug administered
Negress	2:30 p. m.	Positive	
	6 p. m.	Positive	
	11 p. m.	Positive	
	10 a. m.	Negative	
	8 p. m.	Negative	
	9 p. m.	Negative	Discharged

31.2 cc., or 2.2 Gm., of the drug. The rapidity of the disappearance of lesions compared favorably with results reported as following the use of arsphenamine, neoarsphenamine and mapharsen. In 10 patients a negative Kahn reaction was obtained in an average of ten weeks. Only in 1 case were we unable to reverse the Kahn reaction in a patient who had been under treatment for more than fifty-two weeks.

EFFECT ON SECONDARY SYPHILIS

The following results of treatment in patients presenting secondary manifestations of the disease were obtained: The cutaneous manifestations were rapidly cleared, and in the majority of cases they disappeared entirely in an average of fourteen to sixteen days. On an average, treatment for twenty-two weeks was followed by a negative Kahn reaction, the shortest period of treatment resulting in a negative reaction being ten weeks and the longest thirty-four weeks. In 1 case there was a persistent positive Kahn reaction after fourteen months and in another after twelve months of treatment. A persistent weakly positive reaction was noted in a third patient after nine months of treatment.

In our series of 24 patients with secondary syphilis there was no instance of clinical or serologic relapse.

EFFECT ON LATENT AND TERTIARY SYPHILIS

Under the heading of latent syphilis are included all patients who were asymptomatic on admission but in whom a diagnosis of syphilis was made from a positive reaction to a Kahn test of the blood during a routine check in any of the departments of the clinic. Furthermore, there are included in this group a few adults in whom a diagnosis of congenital syphilis was made.

The treatment of this group of 48 patients with acetylglycarsenobenzene was not more productive of reversals of the Kahn reaction than has been our experience with arsphenamine, neoarsphenamine or mapharsen. The total number of reversals of the Kahn reaction was 11, or about 22.4 per cent. Again, as in the cases of secondary syphilis, we did not encounter any serologic relapse in this group. However, none of these patients has had a rest period during which all medication was stopped, and as it is possible that in such a period there might be remissions, a conclusive statement cannot be made until further studies have been completed. It may be said at this time that lesions of the skin and mucous membrane apparently disappeared as rapidly after the administration of this drug as after that of the other arsenicals. It was not so much the object of our investigation to determine whether or not acetylglycarsenobenzene was a more effective drug than the recognized arsenicals as it was to determine if this preparation could be well tolerated when given intramuscularly over a long period. Continued intramuscular injections of acetylglycarsenobenzene over periods up to two years did not produce apparent tissue damage.

EXAMINATION OF THE SPINAL FLUID

The spinal fluid of 64 patients under treatment was examined. A number refused spinal puncture, and several objected to a second examination. However, 23 of the 64 patients were given a second examination. Of the 11 who had a positive result at the first examination, 6 had negative results at the second examination. In 5 persons whose spinal fluid gave a positive reaction on the first examination the reaction remained positive. Two patients whose spinal fluid gave a negative reaction on first examination had a positive reaction at the end of the two year period. The remaining 10 patients who had negative results at the first examination of spinal fluid had negative results at the second examination. It is interesting to note that there seems to be no correlation between the results of examination of spinal fluid and the Kahn reaction of the blood.

SUMMARY AND CONCLUSIONS

Acetylglycarsenobenzene (3,4′-diacetylamino-4 hydroxyarsenobenzene-2′ sodium glycolate) has been studied for two years in the department of dermatology of the University of Pittsburgh. While some observers have previously given the preparation intravenously, our work has been confined to its intramuscular application. The clinical study was restricted to a selected group of patients who had never before received antisyphilitic treatment and in whose cases the diagnosis of syphilis was confirmed either by dark field examination or by serologic test. The spirocheticidal activity of acetylglycarsenobenzene is shown by its rapid effect on the spirochetes in the primary lesions and the

TABLE 3.—*Summary of Results of Two Years' Study*

Total patients treated	84
Total doses of acetylglycarsenobenzene	2,100
Total doses of bismuth compound	1,656
Total doses of mercury	1,432
Total patients with serologic reactions still positive	43
Total patients with negative serologic reactions	41
Total per cent of reactions rendered negative	48.9
Primary Syphilis	
Total number of cases	12
Positive Kahn reactions	2
Negative Kahn reactions	10
Per cent negative reactions	83.3
Secondary Syphilis	
Total number of cases	24
Positive Kahn reactions	4
Negative Kahn reactions	20
Per cent negative reactions	83.3
Latent Syphilis	
Total number of cases	48
Positive Kahn reactions	37
Negative Kahn reactions	11
Per cent negative reactions	22.9

prompt disappearance of secondary lesions. A reversal of serologic reactions from negative to positive after treatment has not been observed, nor has clinical relapse occurred. A recapitulation of our two years' study is shown in table 3.

A study of our data shows that the therapeutic results obtained with acetylglycarsenobenzene are approximately equivalent to the reported results with mapharsen. As to the comparative therapeutic efficiency, only years of continued use of the drug on a wider basis will yield convincing data.

The primary object of this study, however, was to ascertain if the drug could be given with comparative safety for a long time by the intramuscular route. After two years' observation, we believe that with reference to local tolerance this is established.

Nitritoid reactions did not occur, but exfoliative dermatitis was observed. The incidence of the latter was much greater than with other

known arsenicals. The high incidence of toxic manifestations other than dermatitis reported by a number of foreign observers has not been observed by us.

From our preliminary studies we believe that acetylglycarsenobenzene is not to be recommended for general use. The incidence of toxic manifestations, such as dermatitis, must be materially lowered. Perhaps, as in the case of arsphenamine, the manufacturers will be able to lower the toxicity by a modification of the chemical formula, so that eventually the drug may be administered with reasonable safety as well as with therapeutic effectiveness.

ABSTRACT OF DISCUSSION

Dr. Harry M. Robinson, Baltimore: In my clinic at the University of Maryland acetylglycarsenobenzene has been under investigation for ten months. Patients have been treated with courses of twelve weekly intramuscular injections (each dose 6 cc. [0.42 Gm.]) alternating with twelve intramuscular injections of a 10 per cent solution of bismuth camphenilanate in olive oil. There are no rest periods. All patients were ambulatory.

We have treated 88 patients, 7 white persons and 81 Negroes. Sixteen had primary syphilis, of whom 2 had negative serologic reactions; 36 had secondary syphilis; 19 had syphilis during pregnancy, in 5 of these the condition was in the early stages, and they are included in the group with early syphilis, and 19 had congenital syphilis, 3 in the early active stage, 3 in the early latent stage, 3 in the late active stage and 10 in the late latent stage.

In the patients with primary and moist secondary lesions, the spirocheticidal time varied from eight to one hundred and seventy hours.

Eleven patients with moist early lesions gave negative results on dark field examination in twenty-four hours or less, 4 in from twenty-five to thirty-six hours, 7 in forty-eight hours and 3 in seventy-two hours. Reversal of the serologic reaction in patients with early syphilis after the administration of acetylglycarsenobenzene was, in our experience, somewhat slower and less frequently accomplished than with other arsphenamine products.

The involution time of primary lesions averaged twenty-five and five-tenths days, and that of secondary lesions, eighteen and four-tenths days.

In this series there were no serologic or clinical relapses.

In the 10 cases of syphilis during pregnancy in which the outcome is so far known, there were a criminal abortion, a spontaneous miscarriage at seven months, a premature syphilitic stillborn child, a patient who died of hemorrhagic encephalitis at the sixth month of pregnancy and 6 viable children. Serologic tests for syphilis on the 6 viable infants seven to fourteen weeks after birth gave negative results, and there were no clinical signs of syphilis.

Like Dr. Guy and his co-workers, I am convinced that acetylglycarsenobenezene is a potent antisyphilitic drug, capable of intramuscular administration. However, equally important with its therapeutic potency is the question of its toxicity.

Local pain was not a serious factor. Mild gastrointestinal reactions occurred in 8 patients. One patient had slight albuminuria and microscopic hematuria after the seventh injection; this was observed during routine urinalysis. There was no clinical evidence of impairment of renal function. Treatment was discontinued. One week later the urine was normal. In a patient with hypertensive cardiovascular

disease, it seemed that precordial pain and dyspnea were precipitated by the drug, and treatment was discontinued. In 1 case jaundice appeared after the sixth injection. Treatment was discontinued, but later, after twelve weeks of bismuth therapy, the jaundice cleared up and treatment with acetylglycarsenobenzene was resumed without ill effects.

Studies of the blood were made for 30 patients before treatment and after the tenth injection, but none showed any abnormality. Icteric indexes were obtained for 8 patients at some time during the course of arsenical treatment but were within normal limits.

Fatal hemorrhagic encephalitis developed in 1 of the pregnant patients after the second treatment. At autopsy she was found also to have hypernephroma. Cutaneous reactions occurred in 5 of our patients. The eruption in 1 was eczematous, with about seven small lesions, limited to the buttocks, surrounding the sites of injections. Another whose eruption began on the buttocks later had lesions of the fixed type on the thighs and neck. A third patient had an erythematous eruption, especially marked about a vaccination scar and around the site of injection of the drug. There was a case of exfoliative dermatitis which began as a lichen-planus-like eruption and which, although no further arsenical was given, changed to an exfoliative dermatitis. I include in this group a fifth case, one of erythema of the ninth day.

In my experience, acetylglycarsenobenzene has adequate therapeutic efficacy, almost comparable to that of other arsphenamine products. Nevertheless, the advantage of the intramuscular route of administration would more than compensate for its slightly lower therapeutic efficiency were it not for the incidence of serious reactions observed. In the 172 patients of Dr. Guy's series combined with my own there were 16 actually or potentially serious reactions, including 1 death. This suggests that in its present form, at least, acetylglycarsenobenzene may be too reactive as an antisyphilitic drug, and further attempts should be made to change the drug in order to obviate these reactions.

Dr. Joseph Earle Moore, Baltimore: We have used this drug at the Johns Hopkins Hospital and can confirm completely the report made by Dr. Guy.

The manner in which the study of this arsenical drug has been approached is a model of correct procedure. Not satisfied with the experimental data as to toxicity and therapeutic efficiency emanating from Germany, the pharmaceutic house interested in the drug has first carefully repeated these and other experiments in its own laboratories, and the results have also been checked in an experimental laboratory at the Johns Hopkins Hospital. Then, with no idea of releasing the drug for general use unless the laboratory data were confirmed by careful clinical experience, the cooperation of several large clinics, including that of the Johns Hopkins Hospital, was enlisted.

The fundamental idea justifying detailed study of this preparation was the fact that, except for sulfarsphenamine, it is the only trivalent arsenical drug capable of intramuscular administration. If it proved to be as good, or even not quite as good, from clinical standpoints of therapeutic efficiency and toxicity, as the trivalent arsenicals administered intravenously, a great step forward would have been made, because of the technical ease of its administration. Unfortunately, this proved not to be the case. Though it has a fair degree of therapeutic efficiency, the incidence of serious toxic reactions is so high as to make its further use impossible. Unfortunately, also, the serious reactions observed are of types which occur only in human beings, not in experimental animals.

In the combined series of 235 patients from the three clinics of the University of Pittsburgh, the University of Maryland and the Johns Hopkins Hospital, there have been 28 serious reactions. Sensitization dermatitis developed in 18 patients, arsenical jaundice in 3, blood dyscrasias of one or another type in 5, severe nephrosis in 1 and hemorrhagic encephalitis in 1, the last patient dying. This is an incidence of nearly 12 per cent of serious reactions, so far above that observed with other arsenical drugs as to justify the immediate abandonment of the use of this one.

Disappointing as this result may be, the search for a potent and safe arsenical drug for intramuscular administration should certainly continue.

Dr. William H. Guy, Pittsburgh: It is my belief that the most valuable ingredient of any drug or manufactured substance is the integrity of the manufacturer. We have been delighted with the attitude of the firm that asked us to do this work. At no time has there been any suggestion of concealing bad results. They gave us the drug and told us, "Use it and tell us what you find out about it." Nor was any question raised when it was determined finally that the drug would be adversely recommended. I feel that one is justified under these circumstances in recommending that such a procedure be carried on in the investigation of drugs in the future.

ACUTE DISSEMINATED LUPUS ERYTHEMATOSUS

ITS TREATMENT WITH SULFANILAMIDE AND ALLIED PRODUCTS

UDO J. WILE, M.D.
Professor of Dermatology and Syphilology
AND
HERBERT H. HOLMAN, M.D.
Instructor in Dermatology and Syphilology
ANN ARBOR, MICH.

The cause of acute disseminated lupus erythematosus is still obscure. The clinical picture, characterized by septic temperature, prostration, leukopenia, splenomegaly, arthralgia, albuminuria, microscopic hematuria and an invariably fatal termination, offers at least suggestive evidence that infection, whether focal or systemic, is an important etiologic factor. This deduction, perhaps, offers more justification for the use of sulfanilamide and products allied to it in therapy than is found in many other conditions subjected to this therapy during the phase of hyperenthusiasm invariably encountered during the early use of any newly described therapeutic agent.

Conflicting reports are noted in the literature regarding the therapeutic efficacy of sulfanilamide in acute disseminated lupus erythematosus. Wollenberg [1] reported improvement in a case of exanthematous acute disseminated lupus erythematosus. Anderson [2] reported spectacular recovery in a case of acute disseminated lupus erythematosus in which dissemination occurred in a discoid type of lupus erythematosus after undue exposure to sunlight and during therapy with gold sodium thiosulfate. Abramowitz [3] reported improvement in 3 cases of acute disseminated lupus erythematosus. Bloom [4] reported indifferent results in 5 or 6 cases of lupus erythematosus. Sulzberger [5] reported indifferent

From the Department of Dermatology and Syphilology, service of Dr. U. J. Wile, University of Michigan Medical School.

1. Wollenberg, R. A. C.: Lupus Erythematosus Disseminatus, Arch. Dermat. & Syph. **38**:295 (Aug.) 1938.

2. Anderson, H. F.: Fulminating Acute Lupus Erythematosus Cured by Sulfanilamide, Arch. Dermat. & Syph. **38**:621 (Oct.) 1938.

3. Abramowitz, E. W., in discussion on Wise, F.: Discoid Lupus Erythematosus Undergoing Dissemination, Arch. Dermat. & Syph. **38**:661 (Oct.) 1938.

4. Bloom, D., in discussion on Wise, F.: Discoid Lupus Erythematosus Undergoing Dissemination, Arch. Dermat. & Syph. **38**:661 (Oct.) 1938.

5. Sulzberger, M. B.: Lupus Erythematosus Treated with Sulfanilamide, Arch. Dermat. & Syph. **39**:610 (March) 1939.

results in 2 cases of discoid disseminated lupus erythematosus. Cornbleet [6] reported poor results in the treatment of disseminated lupus erythematosus. Weiner [7] reported the use of sulfanilamide in 4 cases of disseminated lupus erythematosus. The first case was one of dissemination of a discoid lupus erythematosus, which was controlled by sulfanilamide. The second case was one of exanthematous subacute disseminated lupus erythematosus, which was arrested by sulfanilamide therapy. The last 2 cases were examples of the exanthematous type of acute disseminated lupus erythematosus, which progressed to fatal termination in spite of sulfanilamide therapy.

We have been given the opportunity of observing the effect of sulfanilamide and allied products in 7 cases of acute disseminated lupus erythematosus.

REPORT OF CASES

CASE 1.—E. T., a 22 year old white unmarried woman, entered the University Hospital on Sept. 15, 1937. The history revealed that her eruption had persisted intermittently for five years, with onset usually in the summer and remission with the advent of winter. Two years prior to admission, the patient noted the appearance on her legs of large blisters, which had responded promptly to local therapy. The eruption which she presented on admission appeared first in May 1937, disappeared during June and July and reappeared in August, from which time it had persisted. She had been treated previous to admission with various ointments and lotions and also by ultraviolet irradiation, which made the lesions worse. Pain in the joints had been present for ten days prior to admission.

Initial examination revealed that the patient was well nourished and well developed but acutely ill. Her temperature was 100.2 F., her pulse rate 96 and her respiratory rate 24. Examination of the skin revealed an eruption confined to the head, neck, upper extremities and anterior surfaces of the legs. The face was universally involved by a purplish, dusky erythema, with superimposed coarse, easily removable scales. Vesiculation was present at the angles of the mouth. There was edema of the face and eyelids. This process extended down over the neck and involved the upper part of the chest. Seven eighths of the cutaneous surface of the arms was involved by discrete and confluent erythema with superimposed scales. There were also areas of loosely adherent, necrotic epithelium, which had apparently followed previous vesiculation. Some of these lesions presented impetiginous crusting. The extensor interarticular surfaces of the fingers presented dully erythematous macular lesions. The palms were involved by the erythematous scaling process present on the arms. The anterior surfaces of the legs showed discrete and confluent erythematous maculopapular lesions.

The mouth showed an inflammatory reaction in the gums but no ulceration. Pea-sized to bean-sized, nontender cervical and inguinal lymph nodes were palpable.

---

6. Cornbleet, T., in discussion on Ebert, M. H., and Omens, D. V.: Lupus Erythematosus Disseminatus Subacutus, Arch. Dermat. & Syph. **39**:372 (Feb.) 1939.

7. Weiner, A. L.: Disseminated Lupus Erythematosus Treated by Sulfanilamide, Arch. Dermat. & Syph. **41**:534 (March) 1940.

The lungs were normal. The heart was not enlarged, and no murmurs were detected. The blood pressure was 125 systolic and 80 diastolic. The liver and spleen were not palpable.

Laboratory Studies.—The blood count studied at the Simpson Memorial Institute for Blood Diseases revealed 60 per cent (9.8 Gm.) hemoglobin by the Sahli method and 3,540,000 red blood cells and 2,650 white blood cells per cubic millimeter. A differential smear showed 74 per cent polymorphonuclear leukocytes, 8 per cent large lymphocytes, 3 per cent small lymphocytes and 15 per cent monocytes. The red blood cells were moderately irregular in size and shape but well colored. There were basophilic granulations in the leukocytes. The platelets were normal in number. The interpretation of this blood picture was "toxic depression of all the blood elements." The urine was normal. The Kahn test of the blood gave a negative result. The result of a tuberculin test was negative. Blood cultures were negative on September 17 and October 2.

Hospital Course.—The patient was slightly improved by bland therapy to the skin. Quinine sulfate was given for twelve days, without improvement, and its administration was discontinued owing to severe tinnitus. Up to this time the total white blood cell count had never been above 3,400 per cubic millimeter. The temperature ranged from 100.2 F. on admission to 103.8 F. on October 16.

Therapy with sulfanilamide was started on October 20. At this time, the patient was acutely ill. The skin, although the intensity of its reaction was considerably diminished, was still severely involved, particularly at the periphery of the previously involved areas. The borders of the older lesions were definitely elevated and acutely erythematous. Her temperature was 103.6 F., pulse rate 118 and respiratory rate 23. Between October 20 and 25 the patient received 20 Gm. of sulfanilamide. On October 21 the temperature reached a peak of 104.6 F. and then dropped abruptly to 98 F. on October 22, only to picket to 103.4 F. on the same day. The temperature returned to normal the following day. On October 24 the temperature reached a peak of 101.4 F.. The patient then received a transfusion of 500 cc. of whole blood. The next day the temperature was 99.4 F., and there was marked clinical improvement. The erythema in the skin faded perceptibly, and on October 28 the borders of the lesions were no longer elevated. The temperature was low until her discharge on October 31.

It was learned in a recent inquiry that this patient suffered a recurrence of her condition and died early in 1939. Unfortunately the circumstances which attended her demise could not be ascertained.

Case 2.—O. B., an 18 year old single white girl, was admitted to the University Hospital on March 22, 1938, with an eruption which had its onset six weeks previously. At its onset the eruption was mildly pruritic and confined to the arms. It was treated by the application of dry calcium phosphate and by internal medication. While she was taking this medication the eyelids and surrounding skin became edematous and reddened, and the eruption on the arms, more extensive. It was noted at this time that the patient's finger tips became cyanotic while dependent. The patient added the information that this had occurred for as long as she could remember, particularly in cold weather.

In December 1933 a doubtful reaction to a blood test had been noted, and the patient had received considerable antisyphilitic therapy in the form of neoarsphenamine and thio-bismol. The Kahn reaction of the blood was negative in 1934 and remained negative. The family history was not significant.

Initial examination revealed that the patient was well nourished and well developed and did not appear acutely ill. The skin presented a generalized eruption which spared the legs. The eyelids were swollen and erythematous. On the arms, thighs and back the eruption was characterized by dull, blotchy maculopapular erythema, which in some areas formed noninfiltrated plaques by confluence of the papules.

General examination revealed acute tonsillitis and periapical abscesses. There was no lymphadenopathy. The heart and lungs were normal. The liver and spleen could not be palpated. The extremities appeared to be edematous but did not pit on pressure. Definite acrocyanosis was noted when the extremities were dependent for a short period.

Laboratory Studies.—The urine was normal. Complete study of the blood, performed at the Simpson Memorial Institute for Blood Diseases, revealed 3,940,000 red blood cells and 5,200 white blood cells per cubic millimeter and 72 per cent (11.7 Gm.) hemoglobin by the Sahli method. A differential smear showed 69 per cent polymorphonuclear leukocytes, 20 per cent large lymphocytes, 7 per cent small lymphocytes and 4 per cent monocytes. No eosinophils were seen, thus ruling out a previously tenable diagnosis of trichinosis. The platelets were adequate in number. The total white blood cell count never exceeded 8,600 per cubic millimeter.

Hospital Course.—The patient was admitted to the dermatologic ward with a diagnosis of erythema multiforme and was given saline catharsis, calcium gluconate orally and bland therapy to the skin. With this regimen the skin showed definite improvement with the exception of the eyelids, which failed to respond to local therapy.

Shortly after admission the patient began to complain of generalized muscular aches and pain in the joints. The temperature was elevated almost constantly from March 27 to July 1, the day of discharge. The character of the temperature varied from constant elevation between 100 and 102 F. to occasional picket fence type, with peaks of over 104 F.

On April 13 sulfanilamide therapy was instituted, and the patient received a total of 10 Gm. of this drug, without any change in the clinical picture. The administration of sulfanilamide was discontinued on April 16.

On April 23 the administration of quinine sulfate was started, and some improvement was noted, in that pains in the muscles and joints partially subsided and the cutaneous lesions faded somewhat, although the erythematous puffiness around the eyes persisted and the temperature was still elevated. The dose of quinine was gradually diminished, and its administration was finally stopped on April 28, since the patient complained of tinnitus. At this time suggestive purpuric lesions were noted on the palms and soles. After this there was an exacerbation of the entire process, with increase in pain in the joints and in depth of erythema, and about this time edema of the vulva was first noted. Subsequent to this exacerbation the cutaneous lesions became definitely dusky in hue. The temperature remained elevated as high as 103 F. An abscessed tooth was removed, without any change in the condition. Quinine sulfate was again given for four or five days, without appreciable effect.

On May 18 a biopsy of muscle and skin from the thigh was performed, with the following report:

"The skin is without inflammatory foci. No vascular lesion is found. There are some edema and serous atrophy of the panniculus. The voluntary muscle shows no significant inflammatory infiltrations or vascular lesions. The changes seen do not suggest dermatomyositis. There is no evidence of trichinosis. The

muscle does show, however, other marked changes. There is some replacement by adipose tissue, and throughout the muscle there are a great many degenerating and atrophic fibers. Consideration of the muscle apart from the history would favor a diagnosis of some acutely progressing muscular dystrophy."

On May 25 the patient received her first intravenous injection of 10 mg. of gold sodium thiosulfate, with subsequent improvement in her condition. The erythema and puffiness of the face subsided to a great extent. The eruption on the body was characterized at this time by a brawny pigmentation with mild scaling. The site of the removal of tissue for biopsy failed to heal by primary intention but rather became a slough, which gradually granulated from the base. The edema of the vulva was decidedly diminished. During the next six weeks the patient received six intravenous injections of gold sodium thiosulfate, the maximum dose being 20 mg. Improvement continued with the exception of one slight exacerbation. The hair of the scalp fell out rapidly. The pigmentation of the skin began to fade slowly. The temperature assumed normal levels for short periods. On June 24 a blood culture showed no growth.

In view of the fact that the patient was unhappy and actually despondent over the long hospitalization, she was discharged for a short time on July 1, 1938. She never returned, as requested, for check-up examination.

Information received recently from a capable dermatologist revealed that the patient consulted him for treatment of a cutaneous condition which he diagnosed as lupus erythematosus.

Case 3.—M. S., a married white woman aged 47, entered the University Hospital on Nov. 22, 1938, as a private patient of one of us (U. J. W.). Her history revealed that the eruption had its onset in May. At that time the patient noted the appearance of split pea-sized to coin-sized erythematous maculopapular lesions on the face and arms. These lesions did not respond to local therapy. In September the patient consulted one of us (U. J. W.), who made a diagnosis of disseminated lupus erythematosus. She was given three intravenous injections of a colloidal gold preparation at weekly intervals. After these injections she suffered a general physical decline and was unable to travel to Ann Arbor, a distance of 20 miles (32 kilometers), for further treatment. She then received three or four intravenous injections of sodium thiosulfate. Three weeks prior to admission albumin was noticed in the urine. At that time the patient complained of noninflammatory edema of the face. The albuminuria persisted during the ensuing three weeks and was associated with great prostration and an increase in the severity of the cutaneous manifestations. Two months prior to admission the patient complained of blurring of vision and headaches, which were usually relieved by acetylsalicylic acid. She was told then that her blood pressure was elevated.

The past history revealed the intermittent presence of migratory arthritis, with pain, redness and swelling involving the ankles, wrists, elbows, hips and fingers, on different occasions. The involved joints always manifested a residual deformity after the subsidence of the acute process.

Two years previous to admission roentgenologic studies revealed nonvisualization of the gallbladder. The menstrual cycle had been normal until recently, when slight irregularity appeared.

Initial examination revealed that the patient was somewhat obese and chronically ill. Her temperature was 98 F. on admission but became elevated to 100 F. during the first day in the hospital. Her pulse rate was 80 and the respiratory rate 20. There was a brightly inflammatory eruption involving the face, neck, chest, back, shoulders and arms. There were some fissuring and weeping on the

neck and definite edema of the neck, of the lower part of the face and of the eyelids. The forearms presented discrete crusted maculopapular lesions, 2 to 3 cm. in diameter. There were some maceration and fissuring on the arms. There were no lesions on the mucous membranes.

The liver and spleen could not be palpated. Her blood pressure was 170 systolic and 110 diastolic.

Laboratory Study.—The urine showed a 4 plus reaction for albumin and no sugar. Microscopic examination of the urinary sediment revealed 10 to 15 red blood cells, 20 to 25 white blood cells and 10 to 15 granular casts. A complete blood count revealed 78 per cent (11 Gm.) of hemoglobin by the Sahli method and 4,200,000 red blood cells and 4,200 white blood cells per cubic millimeter. The red blood cells were normal in size, shape and color. A differential leukocyte count revealed 65 per cent polymorphonuclear leukocytes, 10 per cent eosinophils, 18 per cent lymphocytes and 7 per cent monocytes. The Kahn test of the blood gave a negative result.

Hospital Course.—The patient was first treated with bland local therapy. She was examined in consultation with members of the department of internal medicine, and a diagnosis of acute glomerular nephritis was made. It was felt that sulfanilamide could be used, with careful observation of the patient's renal function. At that time urea clearance studies showed 50 per cent clearance. The patient received during the ensuing seven days 27 Gm. of sulfanilamide. After three days of sulfanilamide therapy, with the sulfanilamide level of the blood 10.5 mg. per hundred cubic centimeters, there was distinct improvement in the condition of the skin. The blood pressure was 145 systolic and 90 diastolic. On the sixth day of sulfanilamide therapy the urea clearance was reported as 36 per cent and the nonprotein nitrogen content of the blood was 35 mg. per hundred cubic centimeters. The patient manifested some intolerance to the drug in the form of headache, nausea and cyanosis. The patient received quinine sulfate during the entire period of hospitalization.

Some improvement was noted in the renal status, as evidenced by a reduction in the reaction for albumin to 3 plus and a reduction in cellular content (0 to 3 red blood cells, 0 to 5 white blood cells and only occasional granular casts). The patient was discharged after eighteen days of hospitalization, with distinct improvement both in the condition of the skin and in general physical condition.

The patient suffered only one mild recurrence of symptoms in the last eighteen months.

Case 4.—J. C., a white housewife aged 27, entered the medical service of the University of Michigan Hospital on Dec. 6, 1938, with a chief complaint of cutaneous rash. The onset of her difficulty occurred four or five years previously, at which time she underwent a nasal operation which involved scraping of the nasal bones. Subsequent to this time she noted a slow, but steady, loss of weight from her normal weight of 140 pounds (63.5 Kg.). Two years prior to admission there occurred progressive weakness and frequent episodes of sore throat of one or two weeks' duration and also multiple episodes of pain in the joints with local heat, redness and swelling, which lasted from a few hours to a few days and then disappeared without residual deformity. She noted a low grade fever associated with these episodes. Seven or eight months ago she first noted the appearance of a severe eruption on the face, neck and trunk. The eruption gradually subsided, but there remained in the flush area of the face a scaling erythema which persisted until the day of admission. During the spring and summer of 1938 she noted mild episodes of fever, and one month before admission

she suffered a severe recurrence of symptoms, which included fever, general malaise, mild headaches, rheumatic pains in the shoulders and other joints and severe edema of the hands and face, particularly in the periorbital regions. There was some diminution of vision. A sore throat appeared and was associated with a cough which was productive of small amounts of purulent sputum. Frequent epistaxes occurred. Her temperature ranged from 100 to 103 F. daily for one month prior to admission. There were also anorexia and occasional nausea and vomiting. Four days before admission the patient first noted pain in the lower part of the abdomen, which gradually localized to a point lateral to McBurney's point. She was treated conservatively for questionable appendicitis, and the abdominal pain gradually subsided. She received a blood transfusion one week before admission, without apparent benefit.

She had never had rheumatic fever or chorea. There was a history of pneumonia and of questionable meningitis when the patient was 2 years old, which left her partially deaf.

Examination on admission showed the patient to be both chronically and acutely ill. The temperature was 103 F., the pulse rate 100 and the respiratory rate 18. Her blood pressure was 110 systolic and 80 diastolic. The skin presented scaling erythema of the flush area of the face, in association with definite periorbital edema and erythema. Examination of the ocular fundi revealed toxic retinitis. The tongue was coated. The gums were red and swollen. There were gray, nontenacious exudates present in both tonsillar fossae. The pharynx was reddened and presented streaks of old blood on its surface. The thyroid gland was barely palpable. There were inconstant rales over the hilus and middle part of the right lung. The heart was not enlarged. There was a short systolic murmur at the apex. No diastolic murmurs were heard. There was exquisite tenderness and muscle spasm localized to a point below and lateral to McBurney's point. No masses or viscera were palpable. There was, on digital examination, tenderness high in the right vaginal vault. There was also tenderness on the right side on rectal examination. The lower extremities showed faint erythema and pretibial edema.

Laboratory Study.—Urinalysis on admission revealed a 3 plus reaction for albumin, 0 to 3 red blood cells, 10 to 15 white blood cells and no casts. A complete blood count revealed 65 per cent (10.6 Gm.) hemoglobin by the Sahli method and 2,590,000 red blood cells and 4,650 white blood cells per cubic millimeter. A differential smear showed 50 per cent polymorphonuclear neutrophils, 42 per cent lymphocytes, 2 per cent monocytes and 6 per cent myelocytes. The leukocytes were young cells. Platelets were numerous. A Kahn test of the blood gave a negative result. The nonprotein nitrogen amounted to 35.2 mg. per hundred cubic centimeters. The total amount of protein in the serum was 4.2 per cent, with 1.8 per cent albumin and 2.4 per cent globulin, producing an albumin-globulin ratio of 0.75. The carbon dioxide–combining power of the plasma was 35 volumes per cent. The plasma chlorides were estimated as 504 mg. per hundred cubic centimeters. Urea clearance test readings were 50 and 54 per cent, respectively. Blood cultures showed no growth on four occasions.

Hospital Course.—The patient's condition became exceedingly grave during her first few days in the hospital. The temperature remained septic. There were frequent episodes of emesis and blood-streaked expectoration. There was decided oliguria, with an output of about one-tenth the intake, which was largely parenteral. The patient was periodically irrational and on the third hospital day had a severe clonic convulsion, which endured for four minutes. Lumbar puncture was imme-

diately performed, and 15 cc. of clear spinal fluid under 200 mm. water pressure was withdrawn, which was normal. Immediate improvement followed this procedure, but in spite of this improvement, the patient was put on the "danger list."

Sulfanilamide therapy was first instituted on the fifth day in the hospital and the patient received 36 Gm. of the drug during the ensuing nine days. Five days subsequent to the cessation of the first course of sulfanilamide the patient was symptomatically much improved, although the oral lesions persisted and were a source of great discomfort. The temperature remained septic. The facial and peripheral edema disappeared, and the erythema of the face partially subsided. The patient also received a transfusion of 600 cc. of citrated blood after the administration of sulfanilamide was discontinued.

During the following two weeks the patient improved slowly but steadily. The temperature was never above 101.5 F.; the white blood count had risen to 6,950 per cubic millimeter, and the urine showed no albumin and only 1 or 2 red blood cells. The erythema in the flush area disappeared almost completely, but occasional bullae appeared in the left axilla and on the buttocks. The oral lesions subsided almost completely. The phenolsulfonphthalein test of renal function demonstrated a 15 per cent return of function in the first fifteen minutes and a 25 per cent return at the end of one hour. In this interim the patient received another blood transfusion.

A second course of sulfanilamide therapy was instituted in the hope of producing even further improvement. A total of 79 Gm. of sulfanilamide was given, and the sulfanilamide level in the blood was reported as 14.4 mg. per hundred cubic centimeters. There was subsequent further decrease in temperature, but elevations to about 100 F. occurred daily. The patient was able to leave her bed for short periods. A slight exacerbation in the cutaneous manifestations prompted further sulfanilamide therapy; 78 Gm. was administered, with intolerance manifested in the form of almost constant nausea and headache. The sulfanilamide concentration in the blood was 10.2 mg. per hundred cubic centimeters. The patient became afebrile and remained so in spite of the appearance of new ulcerative lesions on the tongue. These lesions disappeared without further therapy. The patient was then discharged, after being in the hospital ninety-eight days.

The patient was readmitted to the hospital one month later as an emergency patient. She had gained 15 pounds (7 Kg.) up to ten days before admission. At that time she noticed the recurrence of pain, redness and swelling in the elbows, knees, fingers and toes. There had been severe pain in the right lower quadrant of the abdomen, associated with frequent vomiting. Examination revealed the patient to be acutely ill, with a temperature of 104.8 F., a pulse rate of 140 and a respiratory rate of 32. The blood pressure was 95 systolic and 40 diastolic. Erythema was present in the flush area of the face and also on the neck. There was an arcuate ulcer in the midline of the tongue. No murmurs were heard from the heart. There was dulness at the base of the right lung posteriorly, with moist rales, but no alteration in the breath sounds. The abdomen presented a boardlike rigidity, with tenderness throughout. The viscera could not be palpated. Rectal examination revealed a fluctuant mass on the right side. Analysis of catheterized urine revealed a 3 plus reaction for albumin, 30 to 40 red blood cells and 15 to 20 white blood cells and numerous granular and cellular casts. The total white blood cell count was 25,000 per cubic millimeter. The patient was immediately transferred to the surgical service, where a diagnosis of perforated appendix with generalized peritonitis was made. She was treated by the Ochsner regimen and given a 5 per cent solution of dextrose containing 5 Gm.

of sulfanilamide intravenously. A roentgenogram of the chest showed pleuritis of the right base and apex, with probable pneumonitis or bronchopneumonia. The course was steadily downhill, with generalized convulsive seizures, cyanosis, oliguria and uremia, with the nonprotein nitrogen content of the blood 60 mg. per hundred cubic centimeters. Death occurred on the day after admission. Unfortunately, permission for autopsy could not be obtained.

CASE 5.—L. K., a 15 year old white boy, entered the dermatologic service of the University Hospital on March 25, 1939, with a chief complaint of "skin eruption." The eruption had its onset three weeks prior to admission as slightly pruritic, nonexudative, erythematous lesions, which gradually became more widespread until the entire face was involved in an erythematous, edematous process, so severe that at times both eyes were almost closed. Bullous lesions appeared in the mouth, ruptured and healed slowly. One week before admission the eruption spread to involve the dorsa of the hands, fingers and outer surfaces of the forearms. There were no pains in the joints or muscles. The patient described a similar attack in November 1937, which lasted about three and one-half weeks and which subsided after several blood transfusions.

There was a history of infantile eczema and of hay fever for five or six years. The family history was not significant.

Initial examination revealed the boy to be well nourished, well developed and taller than one would expect for his age. His temperature was 101.8 F., his pulse rate 112 and his respiratory rate 25. He presented an eruption confined to the face, the upper part of the chest and the arms. There was severe edema of the face, sufficient to almost close both eyes. The ears and lips were also distinctly edematous. The entire face, ears and V of the neck were characterized by the presence of a bluish red, dusky erythema, with superimposed fine, dry scales. On the dorsal surfaces of the arms and the upper part of the chest were numerous discrete, pea-sized to bean-sized, slightly raised, erythematous lesions, some of which appeared to be vesicular. The mouth presented numerous erosive and ulcerative lesions, with gray or yellow pellicles scattered over the hard palate, tongue and labial and buccal mucosae. The heart rate was rapid, and the first pulmonic sound was harsh, while the second sound was accentuated. A soft systolic murmur was heard over the apex. The blood pressure was 110 systolic and 60 diastolic. The liver and spleen were not palpable. The physical examination otherwise gave negative results.

Laboratory Study.—The urine was completely normal on admission and remained so until April 15, at which time there was a 1 plus reaction for albumin, no red blood cells or casts, and 2 to 3 white blood cells per high power field. A blood count showed 103 per cent (16.8 Gm.) hemoglobin by the Sahli method and 4,600,000 erythrocytes and 3,900 leukocytes per cubic millimeter. A differential smear revealed 64 per cent polymorphonuclear leukocytes, 34 per cent lymphocytes and 2 per cent monocytes. Platelets were abundant. During the course of hospitalization, in spite of blood transfusions, the hemoglobin dropped to 82 per cent (13.4 Gm.), and the total white blood cell count varied, attaining a peak of 9,300, but never dropping lower than the admission count of 3,900 per cubic millimeter. A blood culture was negative. A Kahn test of the blood gave a negative result. A roentgenogram of the chest revealed pleural thickening.

Hospital Course.—The patient received bland local therapy to the skin and a small blood transfusion. Sulfanilamide therapy was instituted on the fourth hospital day, and the patient received 22 Gm. in the next six days. Although the edema of the face subsided to a slight extent and the patient felt slightly

better, the temperature was elevated daily to 102 F. Purpuric lesions appeared on the arms and legs. His condition became slowly but steadily worse, with increase in temperature to 104 F. and the appearance of new lesions around the lips and in the mouth. He was presented at a meeting of the Detroit Dermatological Society, at which time the visiting dermatologists concurred in the diagnosis of acute disseminated lupus erythematosus.

Therapy with sulfapyridine was instituted on the eighteenth hospital day, and 21 Gm. of this drug was given in the ensuing six days. Another blood transfusion was given during the course of sulfapyridine therapy. In spite of this medication the course of the patient continued to become steadily worse, with the continuous appearance of new lesions on the extremities, particularly on the tips of the fingers and toes.

The patient's family was informed of the serious nature of the illness but, in spite of this, insisted on the patient's discharge. He was discharged against advice after a hospitalization period of twenty-nine days, at which time his rectal temperature was 106 F.

Communication with the patient's local physician revealed that the course was steadily downhill, in spite of another blood transfusion. Death occurred six days after the patient's discharge. A blood culture taken shortly before death revealed a pure culture of Streptococcus viridans. Permission for autopsy was not obtained.

CASE 6.—J. L., a 28 year old, married white man, entered the University Hospital on April 21, 1939, with a chief complaint of "kidney trouble." He had been well until two months prior to admission, at which time he noted the appearance of swelling around the eyes associated with an eruption which spread across the bridge of the nose onto the cheeks. The eruption persisted with slight dissemination so that the ears and upper part of the back were involved. Three weeks after the onset of the eruption, the patient first noted pains in both ankles, both knees and the muscles around both knees. He also noted a pain in the right lower quadrant of the abdomen, which radiated through to the back. He felt at this time that he was feverish, in that he perspired freely, particularly at night, and frequently awoke in the morning with his sleeping garments moist. He complained of occasional headache and ease of fatigue. Five weeks after the onset of the eruption he noted swelling of both ankles and knees.

The past history was not remarkable, with the exception of traumatic amputation of the entire left upper extremity when he was 5 years of age.

The patient had been married for eighteen months. His wife and a child, aged 7 months, were living and well. His family history was not significant.

Initial examination revealed that he was well developed and well nourished and appeared subacutely ill. The skin presented a discrete and confluent dusky erythematous eruption in a striking "butterfly" distribution on the nose and flush areas of the face, with extension around the eyes, on the forehead and on the ears. Scattered lesions were also noted on the upper part of the back. The lesions were maculopapular, varied in size from that of a glass pinhead to that of a dime and were covered with a fine scale. The erythema did not blanch entirely on pressure. There was edema of both eyelids, with faint erythema. Macular, purpuric lesions were noted on the hard palate. The tonsils had been cleanly removed.

General examination revealed generalized, nontender, bean-sized lymphadenopathy. The lungs were normal. The heart was not enlarged. No murmurs were heard. The blood pressure was 145 systolic and 90 diastolic. The liver and spleen could not be palpated.

Laboratory Study.—The urine on admission showed a 2 plus reaction for albumin, no sugar, 50 to 70 red blood cells, 10 to 15 white blood cells and 15 to 25 granular casts. The blood on admission revealed 78 per cent (11.4 Gm.) hemoglobin and 3,780,000 erythrocytes and 4,020 leukocytes per cubic millimeter. A differential smear showed 68 per cent polymorphonuclear neutrophils, 1 per cent eosinophils, 28 per cent lymphocytes and 3 per cent monocytes. The reaction to a tuberculin test with a dilution of 1:10,000 was negative after forty-eight hours. A roentgenogram of the chest was normal. The result of a Kahn test of the blood was negative. A blood culture showed no growth. The nonprotein nitrogen content of the blood was 41.3 mg. per hundred cubic centimeters on admission. The sedimentation index was 0.54 mm. per minute. A urea clearance test showed 24 per cent and 23 per cent clearance in two specimens.

Hospital Course.—The temperature was 99.5 F., the pulse rate 85 and the respiratory rate 20 on admission to the ward. There was daily elevation of temperature to 100 F. for several days. The patient was given a neutral diet, with 90 Gm. of ammonium chloride daily for three day periods alternating with three day rest periods. The nonprotein nitrogen content of the blood was 60 mg. per hundred cubic centimeters, and the carbon dioxide–combining power of the plasma was 31 volumes per cent on the seventh hospital day. The condition was diagnosed as acidosis and uremia following ammonium chloride therapy. Ammonium chloride therapy was discontinued, and the diet was changed to a salt-poor, low protein diet, and fluids were forced to 4 liters daily. It was deemed wisest to postpone sulfanilamide therapy until the nonprotein nitrogen content of the blood could be reduced. On the tenth day in the hospital the patient became comatose and disoriented, rallied temporarily after the administration of intravenous fluids and again lapsed into coma. The blood pressure was 170 systolic and 100 diastolic. Coma persisted in spite of all therapy, and the nonprotein nitrogen level of the blood rose to 120 mg. per hundred cubic centimeters. Five grams of sulfanilamide were given intravenously on the twelfth and fifteenth hospital days, since it was felt that the situation was hopeless and that nothing but good might be derived from this therapy. Coma persisted in spite of the sulfanilamide, and the course continued steadily downhill. The patient died on the twenty-first hospital day.

Permission for autopsy was obtained, and members of the department of pathology returned as preliminary diagnoses subacute glomerulotubular nephritis, anasarca, acute passive congestion of all organs, lipoidosis of the myocardium, kidneys and liver, far advanced bilateral acute fibrinopurulent lobular pneumonia, splenic and pulmonary infarcts, marked submucosal hemorrhage of the small intestine, acute hemorrhagic pharyngitis, chronic ulcer of the rectum and old calcified tuberculous hilar lymphadenopathy. There were no endocardial vegetations.

Case 7.—I. E., a 19 year old single white woman, was admitted to the University Hospital on Sept. 12, 1939, with a chief complaint of "eruption on the face." She had enjoyed good health until three months prior to admission, at which time painful swelling of the proximal interphalangeal joints of the fingers first developed. Because of this, she consulted her local physician, who found albumin in her urine. The arthralgia of the finger joints was followed in three weeks by similar involvement in the wrists, shoulders and feet. These symptoms endured until one month prior to admission. The patient became progressively weaker. Iron and liver extract were administered to combat anemia which was present. Three weeks prior to admission pleuritic pain developed in the apex of the right lung, which gradually subsided. For three weeks prior to admission she had intermittently "cleared her throat" and expectorated bright red blood. Two weeks

before admission she first noted the appearance of the cutaneous eruption, which progressed gradually until the bridge of the nose and the cheeks were involved in a butterfly distribution. The ears and suprasternal region were also involved. There had been bleeding from the gums and subconjunctional hemorrhages for one day prior to admission.

There was a history of only measles, whooping cough and scarlet fever when she was 4 years of age. Her family history was not significant.

Initial examination revealed a well developed and well nourished woman who appeared acutely ill. The temperature was 102.2 F., the pulse rate 96 and the respiratory rate 20. Her blood pressure was 132 systolic and 70 diastolic. A dusky, blotchy, confluent, macular erythema involved the bridge of the nose and malar eminences in a typical "butterfly" pattern. Similar lesions were also present on the forehead, chin, upper part of the chest and back. The nasal mucosa presented several small areas of superficial ulceration. Both eyes revealed subconjunctival hemorrhages lateral to the corneas. The external appearance of the eyes was otherwise normal. The fundi were normal. The lips were dry and fissured. Evidence of hemorrhage was present in the gingival margins, which were edematous and congested. Petechiae were noted in the buccal mucous membranes, together with superficial ulcerations on the palate and uvula. The lungs were normal. The heart was normal in size. A third heart sound was audible over the apex. There was a soft, blowing systolic murmur heard over both the apex and the base. No diastolic murmur was heard. In the right upper quadrant of the abdomen there was slight tenderness without spasm. The liver and spleen could not be palpated. The reflexes of the upper extremities were sluggish, and those of the lower extremities could not be elicited. There was no edema of the ankle. The joints were normal except for slight tenderness during internal rotation of the shoulder joints. There was a slightly tender, enlarged, right axillary lymph node.

Laboratory Study.—The result of a routine Kahn test of the blood was negative. Repeated urinalyses showed 1 to 3 plus reaction for albumin, occasional to 10 red blood cells, 10 to 15 white blood cells and 10 to 20 coarsely granular casts. A blood count, studied at the Simpson Memorial Institute for Blood Diseases, revealed 3,700,000 erythrocytes and 2,200 leukocytes per cubic millimeter and 59 per cent (9.3 Gm.) hemoglobin. A differential smear showed 82 per cent polymorphonuclear leukocytes, 6 per cent large lymphocytes, 8 per cent small lymphocytes and 4 per cent monocytes. Platelets were decreased in number. These findings were interpreted as being secondary to depression of the bone marrow by toxemia.

These observations remained constant until death, at which time the total white blood count was increased to 8,050 per cubic millimeter. The clotting time, clot retraction time and bleeding time were normal. A blood culture on two occasions gave negative results. Sedimentation rate was 1.3 mm. per minute. A urea clearance test showed 44 per cent and 31 per cent clearance. An electrocardiogram was not definitely abnormal.

Hospital Course.—The patient received supportive therapy in the form of three blood transfusions, ferrous sulfate and supplementary vitamins. Sulfanilamide therapy was instituted on the sixth hospital day, and the patient received 7.5 Gm. of this drug in the ensuing twenty-four hours. Severe nausea necessitated discontinuation of this medication. Therapy with promin[8] was then started, and the

8. Promin is a sulfanilamide derivative developed by Parke, Davis & Co. It is p, p'-diaminodiphenylsulfone-N,N'-di-(dextrose sodium sulfonate).

patient received 32 Gm. of this drug by subcutaneous injection during the next five days. The concentration of promin in the blood reached a peak of 21.5 mg. per hundred cubic centimeters. Response to this medication was indifferent. There was, perhaps, slight improvement in the cutaneous manifestations. The temperature, however, continued to picket daily to 103 F. during the entire period of promin therapy. The spleen was palpably enlarged and tender for the first time on the twelfth hospital day. At no time did the heart show clinical evidence of endocarditis.

Sulfapyridine therapy was instituted on the fifteenth hospital day, and the patient received 13 Gm. of this drug in the next four days. No visible benefit accrued. The patient had great difficulty in ingesting the drug, due to the presence of ulcers in the mouth and throat which bled almost continuously. Blood study at this time revealed 2,200,000 erythrocytes and 4,900 leukocytes per cubic millimeter and 35 per cent (5.6 Gm.) hemoglobin. A differential smear showed 84 per cent polymorphonuclear leukocytes, 9 per cent large lymphocytes, 2 per cent small lymphocytes and 5 per cent monocytes. The red blood cells showed all signs of regeneration. Platelets were adequate. A hematocrit reading was 19.5 per cent. The mean corpuscular volume was 90 cubic microns. It was the opinion of the workers at the Simpson Memorial Institute for Blood Diseases that this blood picture represented hemolytic anemia, conceivably secondary to the sulfapyridine therapy. A transfusion of 650 cc. of citrated blood was given, but in spite of this, the patient's condition continued steadily downhill, and death ensued on October 4, the twenty-third hospital day.

Postmortem examination, limited to the thorax and abdomen, revealed acute tubular nephritis, multiple petechial hemorrhages on the mucous membranes, lungs, conjunctivas and dura, pulmonary edema, terminal bronchopneumonia, generalized hyperplastic lymphadenitis and fatty nutmeg liver.

COMMENT

Unfortunately, the effect of sulfanilamide as the sole therapeutic agent could not be evaluated, since many of the patients received concomitant therapy, such as blood transfusions, quinine or gold sodium thiosulfate. However, since the effect of sulfanilamide on certain of the patients was not beneficial in spite of the other agents utilized, it might be justifiably argued that sulfanilamide was of at least some value in those cases in which it was used in conjunction with other agents and in which definite clinical improvement was noted.

Definite clinical improvement was noted in cases 1, 3 and 4 during the administration of sulfanilamide. In case 3 only one transitory recurrence of symptoms has been noted in the eighteen months since discharge. Case 1 is the same case in which Wollenberg [1] previously reported benefit by sulfanilamide. Death occurred at a later date. In case 4 death was caused by what was probably a recurrence of acute disseminated lupus erythematosus, complicated by an acute condition of the abdomen. In case 2, in which a diagnosis of acute disseminated lupus erythematosus could not be definitely established, there was no improvement after sulfanilamide therapy, but some improvement followed the administration of

gold sodium thiosulfate. In case 5 death occurred after an average trial of both sulfanilamide and sulfapyridine, without any significant improvement. Death occurred in case 6 after a rather poor trial of sulfanilamide, necessitated by severely impaired renal function. In case 7, in spite of therapy with sulfanilamide, promin and sulfapyridine, death occurred. The toxic effect of the latter drug may have been a factor in the death.

It is of interest to note that the only established case of acute disseminated lupus erythematosus herein reported in which improvement has persisted following the use of sulfanilamide was one of the discoid type which had undergone dissemination during therapy with gold sodium thiosulfate. The large majority of cases in which improvement was reported following the use of sulfanilamide were also cases of dissemination of a previously discoid lupus erythematosus. Patients with the exanthematous type of acute disseminated lupus erythematosus occasionally manifested transitory improvement, but the great majority of them ultimately died.

Promin was used in 1 case in which sulfanilamide was not tolerated. Sulfapyridine was used in 2 cases in which sulfanilamide had previously failed therapeutically. Neither of these drugs was found to be of greater therapeutic value than sulfanilamide, although promin was tolerated in a case in which sulfanilamide could not be used.

SUMMARY AND CONCLUSIONS

The therapeutic effect of sulfanilamide, sulfapyridine and promin (p,p′-diaminodiphenylsulfone-N,N′-di-[dextrose sodium sulfonate]) was observed in 7 cases of acute disseminated lupus erythematosus.

Sulfapyridine and promin produced no beneficial results, failing therapeutically where sulfanilamide had previously failed. These drugs were not used in cases in which sulfanilamide was beneficial.

While the results in general are discouraging, the fact that some improvement was manifested in several instances when sulfanilamide was administered warrants its further use in cases of this type. It is certainly as efficacious as the accepted therapeutic agents for this morbid syndrome.

Relatively better results were obtained in cases of discoid disseminated lupus erythematosus than in cases of the exanthematous type of acute disseminated lupus erythematosus.

EXCRETION OF BISMUTH IN THE URINE OF PATIENTS TREATED WITH BISMUTH ETHYLCAMPHORATE

FRANCIS M. THURMON, M.D.
AND
NORBERT BENOTTI, M.S.
BOSTON

At the present time it is generally accepted that after the intramuscular administration of a bismuth compound a large portion of the absorbed metal is excreted in the urine and a smaller portion is excreted in the feces, while the remainder is retained in the tissues for varying periods. In general, it appears that the excretion of bismuth in the urine may be considered to be a fair index of actively circulating bismuth, and this is an indication of the rapidity of its absorption from the muscles. Cole and his co-workers [1] stated that a preparation which furnishes a more or less continuous daily urinary excretion of 2 to 4 mg. or more of bismuth is potentially a valuable antisyphilitic agent.

In choosing a bismuth preparation the physician should consider the indications for each particular patient. An approved aqueous solution of bismuth administered two or three times weekly produces a rapid effect. For a somewhat slower but efficient effect an approved oil-soluble preparation is recommended for five to seven day injection, while for an effect slow in building up but eventually sustained, oil suspensions of bismuth are given once weekly. The insoluble bismuth salts, however, are slowly absorbed and occasionally form reservoirs of bismuth within the muscle.

The physician in choosing a bismuth preparation, should consider that in general the more motile or more rapid the bismuth effect, the greater the potentially toxic effect. Thus, the dosage of the approved aqueous bismuth solution is usually smaller than that of an oil-soluble solution, while the insoluble bismuth in suspension carries the largest dose of all.

This study was aided by a grant from the Upjohn Company, Kalamazoo, Mich.

From the Clinic of Dermatology and Syphilology of The Boston Dispensary, the Chemistry Laboratory of the Joseph H. Pratt Diagnostic Hospital and the Department of Medicine, Tufts College Medical School, units of the New England Medical Center.

1. Cole, H. N.; Sollmann, T.; Henderson, K.; Binkley, G. W.; Connors, H.; Cooper, G.; Lover, W. R.; Riechle, H.; Schwartz, W. F.; Seecof, D., and Sullivan, M.: Choice of Bismuth Preparation: Clinical Résumé of Excretion and Retention Studies, Am. J. Syph., Gonor. & Ven. Dis. **23**:143-149 (March) 1939.

It would seem, then, in view of these well known and generally accepted facts, that an oil-soluble bismuth compound which is therapeutically efficient, which is of low toxicity, which is not sufficiently opaque to cast a shadow detectable by roentgen rays and which, as measured by urinary excretion, produces a rapidly rising peak and a sustained bismuth effect well within the accepted therapeutic range—these factors being true with a dose of 1 cc., or 40 mg., of elemental bismuth, at seven day intervals—merits attention. Bismuth ethylcamphorate is such a compound. The data herein presented are observations on the level of bismuth excreted in the urine of patients treated with this liposoluble preparation.

An earlier paper,[2] a clinical study of bismuth ethylcamphorate, indicated that the drug possessed valuable properties in the treatment of syphilis. In that paper it was stated that the drug possessed a low degree of toxicity for the human subject and that judging by its clinical effectiveness it appeared to possess an optimum rate of absorption and elimination. Continuous clinical experience with its use through the past six years has amply borne out those observations. The present communication on absorption and elimination indicates a rapid absorption and a sustained circulation of bismuth adequate to maintain antisyphilitic levels of bismuth concentration in the body. The data show that a dosage of 40 mg. of elemental bismuth at seven day intervals is sufficient to maintain adequate bismuth in the circulation over sufficient periods for maximum therapeutic effectiveness consistent with lowest toxicity. The data also show that a larger dose (2 cc.) is well tolerated and without nephrotoxic or other unusual untoward effects.

DESCRIPTION OF DRUG

Bismuth ethylcamphorate is a liposoluble bismuth salt of ethyl camphoric acid, having the formula $(C_8H_{14}.COOC)_3Bi$ (23.47 per cent bismuth). It melts at 57 C. and is soluble in oil and oil solvents. The drug is a stable, clear, oily solution, each cubic centimeter containing 40 mg. of elemental bismuth, 0.011 Gm. of camphor and 0.025 cc. of benzyl alcohol dissolved in sweet almond oil. Acute toxicity experiments using albino rats show the minimum lethal dose of bismuth ethylcamphorate to be 250 mg. of metallic bismuth per kilogram of body weight.

METHOD AND MATERIAL

The determination of bismuth was performed by using the photoelectric colorimeter,[3] which has been described. A suitable quantity of urine was wet

2. Thurmon, F. M.: Bismuth Ethyl Camphorate: Clinical Observations on a New Oil Soluble Bismuth in the Treatment of Syphilis, New England J. Med. **215**:315-321 (Aug. 20) 1936.

3. Benotti, N., and Thurmon, F. M.: The Photometric Determination of Bismuth in Urine, J. Invest. Dermat., to be published.

ashed, and the yellow color was developed by means of four times normal potassium iodide. The transmission of the solution was determined by a Cenco photelometer. A calibration curve eliminates standards, and from the transmission percentage the number of milligrams of bismuth was obtained.

The patients used for the study consisted of 9 adults, of whom 7 were male and 2 female. Each patient was hospitalized for a minimum period of three weeks. Daily twenty-four hour collections of urine were made, and specimens were analyzed for the bismuth content. The first twenty-four hour period comprised the control specimen to make sure the urine did not normally contain bismuth. The regular hospital diet was permitted. The patients were allowed to be up and about within the confines of their corridor, but at no time during the study did they leave the hospital. In certain cases the fluid intake was limited to a minimum of 1,200 to 1,500 cc. per twenty-four hours. Roentgenograms of the sites of injection were made in several cases to determine whether the bismuth within the muscle was sufficiently opaque to cast a shadow.

Two patients received a single injection of 2 cc. each. One patient received a single injection of 1 cc., and in this instance the bismuth excretion was followed

Patients Treated with Bismuth Ethylcamphorate

Case Number	Sex	Age, Years	Weight, Pounds	Height, Inches	Treatment With Bismuth Ethylcamphorate
1	Male	31	150.2	61.0	Single injection of 1 cc.
2	Male	34	137.5	71.5	Single injection of 2 cc.
3	Male	47	168.5	66.5	Single injection of 2 cc.
4	Male	45	138.0	67.0	1 cc. each week for three injections
5	Female	58	163.9	64.2	1 cc. each week for three injections
6	Male	59	100.0	63.5	1 cc. each week for three injections
7	Male	49	142.2	67.0	2 cc. each week for three injections
8	Male	52	142.5	66.0	2 cc. each week for three injections
9	Female	48	163.4	67.0	2 cc. each week for three injections

through to its completion. Three patients received the 1 cc. dose at seven day intervals for three injections. Three patients received the 2 cc. dose at seven day intervals for three injections. These patients are listed in the table.

Observations on the fecal excretion of bismuth after the intramuscular administration of bismuth ethylcamphorate are reserved for a possible future publication. Most investigators regard this phase of the study of parentally administered bismuth to be of little consequence as compared with the importance of bismuth excreted in the urine.

ROENTGEN RAY STUDIES

Absorption from the site of injection in the gluteal muscle, as judged by the thinning of the roentgen shadow, could not be accomplished with bismuth ethylcamphorate, because the material was not sufficiently opaque to cast a shadow. In 16 instances roentgenograms of patients receiving bismuth ethylcamphorate failed to show bismuth deposits. In all cases the drug was injected into the gluteal muscle, and each roentgenogram included both buttocks, thus encompassing all sites of injection.

The roentgen ray factors used in making these exposures were a rotating anode tube, 75 kilovolts, 250 milliamperes, and distance, 36 inches (91 cm.), with the Patterson high speed screens.

Two typical case histories follow.

CASE 8.—Observations from Dec. 12 through 27, 1939.

Dec.

12. Before treatment. No roentgenographic evidence of bismuth deposit.
13, 10 a. m. Bismuth ethylcamphorate, 2 cc., administered into right buttock.
13, 3 p. m. Roentgenogram taken, with no evidence of bismuth deposit.
20, 10 a. m. Bismuth ethylcamphorate, 1 cc., administered into right buttock.
20, 10 a. m. Bismuth ethylcamphorate, 1 cc., administered into left buttock.
20, 3 p. m. Roentgenogram taken, with no evidence of bismuth deposits.
27, 10 a. m. Bismuth ethylcamphorate, 2 cc., administered into right buttock.
27, 3 p. m. Roentgenogram taken, with no evidence of bismuth deposit.

CASE 4.—Observations from Dec. 6 through 28, 1939.

Dec.

6. Before treatment. No roentgenographic evidence of bismuth deposit.
7, 10 a. m. Bismuth ethylcamphorate, 1 cc., administered into right buttock.
7, 3 p. m. Roentgenogram taken, with no evidence of bismuth deposit.
8, 3 p. m. Roentgenogram taken, with no evidence of bismuth deposit.
11, 3 p. m. Roentgenogram taken, with no evidence of bismuth deposit.
14, 10 a. m. Bismuth ethylcamphorate, 1 cc., administered into left buttock.
14, 3 p. m. Roentgenogram taken, with no evidence of bismuth deposit.
15, 3 p. m. Roentgenogram taken, with no evidence of bismuth deposit.
18, 3 p. m. Roentgenogram taken, with no evidence of bismuth deposit.
21, 11 a. m. Bismuth ethylcamphorate, 1 cc., administered into left buttock.
22, 3 p. m. Roentgenogram taken, with no evidence of bismuth deposit.
28, 3 p. m. Roentgenogram taken, with no evidence of any dense metallic substance in the buttocks.

These roentgenograms for bismuth deposits were taken at sufficiently varying intervals to detect bismuth within the gluteal muscle had it been there as a metallic substance or as some intermediary compound of sufficient density to cast a shadow. In no instance was a shadow obtained. This seems to indicate an absence of visible bismuth reservoir at the site of injection and a degree of motility making bismuth readily absorbed and available to the tissues. That there is such motility is amply borne out by the data in this paper on bismuth excretion and perhaps, in part at least, explains the excellent therapeutic properties of this preparation.

EXCRETION STUDIES

The data on absorption and elimination of bismuth in the urine following clinical dosage of bismuth ethylcamphorate are illustrated in charts 1 through 9.

The daily excretion of bismuth in the urine of human beings after intramuscular injection of bismuth ethylcamphorate in doses of therapeutic order is characterized by promptness of onset, considerable daily irregularity and long duration.

CASE 1.—The patient received a single injection of 40 mg. of bismuth and within eighteen days excreted 36 per cent of the total amount injected. A twenty-four hour urine specimen obtained forty-two days after the injection of bismuth showed

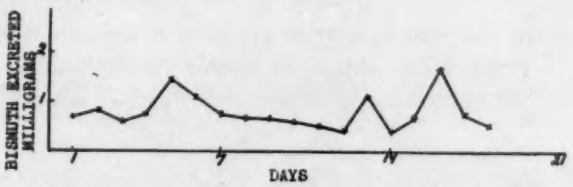


Chart 1 (case 1).—The daily excretion of bismuth in the urine after a single injection of 40 mg. of bismuth (1 cc. bismuth ethylcamphorate). The average daily excretion for the first week was 0.88 mg., for the second week 0.63 mg. and for the third week 0.92 mg. The patient excreted 36 per cent of the total bismuth injected within eighteen days after the treatment.

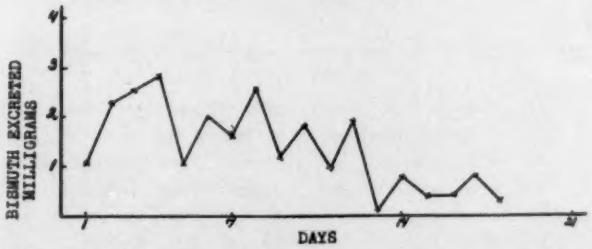


Chart 2 (case 2).—Within eighteen days after a single injection of 80 mg. of bismuth (2 cc. bismuth ethylcamphorate) 30 per cent was excreted in the urine. The average daily bismuth excretion for the first week was 1.79 mg., for the second week 1.32 mg. and for the third week 0.45 mg.

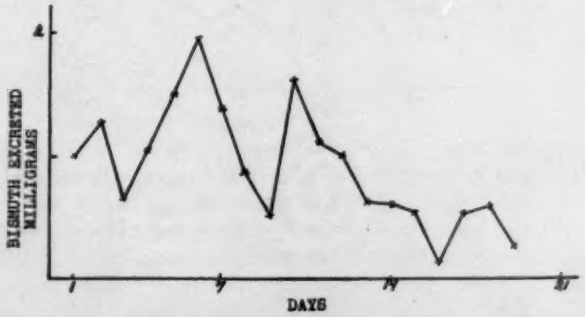


Chart 3 (case 3).—Within nineteen days after a single injection of 80 mg. of bismuth (2 cc. bismuth ethylcamphorate) 20 per cent was excreted in the urine. The average daily excretion of bismuth in the urine was 1.1 mg. for the first week, 0.92 mg. for the second week and 0.41 mg. for the third week.

0.075 mg. of bismuth per 50 cc. of urine. A second specimen, obtained fifty-six days after treatment, contained 0.035 mg. of bismuth per 50 cc. of urine. Another

specimen obtained fifty-six days after injection showed a trace of bismuth, while a final specimen obtained seventy-three days after the single injection showed no bismuth. The known sojourn of bismuth in the body in this particular instance was at least fifty-six days.

The day to day fluctuations of bismuth in the urine were considerable and tended to parallel the output of urine, although as a constant observation this did not hold true. The chart of case 6, amply illustrates this point.

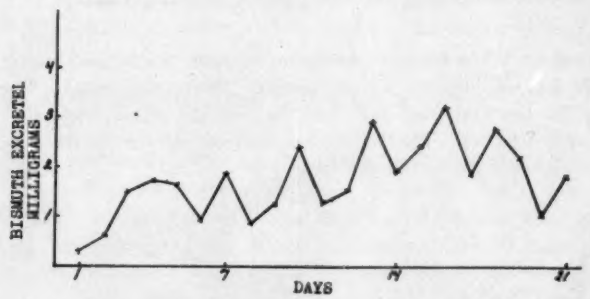


Chart 4 (case 4).—Within three weeks after three injections of 40 mg. of bismuth (1 cc. bismuth ethylcamphorate) at seven day intervals 30 per cent of the total bismuth was recovered in the urine. The average daily bismuth excretion for the first week was 1.23 mg., for the second week 1.73 mg. and for the third week 2.21 mg.

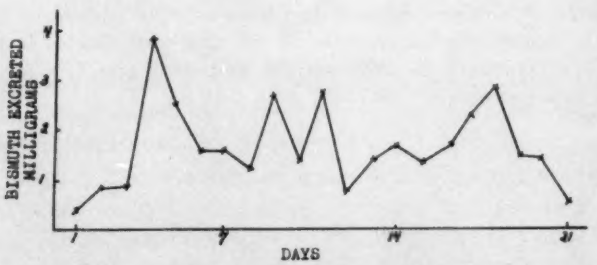


Chart 5 (case 5).—Single injections equivalent to 40 mg. of elemental bismuth (1 cc. bismuth ethylcamphorate) per week were given for three weeks, during which time 29 per cent of the injected bismuth was excreted in the urine. The average daily excretion of bismuth for the first week was 1.73 mg., for the second week 1.74 mg. and for the third week 1.66 mg.

Peaks in the daily average bismuth excretion following single injections were usually attained in the first week and were followed by descending quantities over the study period.

CASE 2.—After a single dose of 80 mg. of bismuth there was an average daily excretion for the first week of 1.79 mg. of bismuth, for the second week of 1.32 mg. and for the third week of 0.45 mg.

In contrast to this, the peaks in the daily average bismuth excretion of patients receiving multiple injections of 40 mg. and 80 mg. of bismuth at seven day intervals showed ascending levels of total or cumulative excretion, the maximum average being attained during the third week in 4 cases.

The total urinary excretion of bismuth in these cases ranged from 17 to 48 per cent within eighteen to twenty-one days following the first

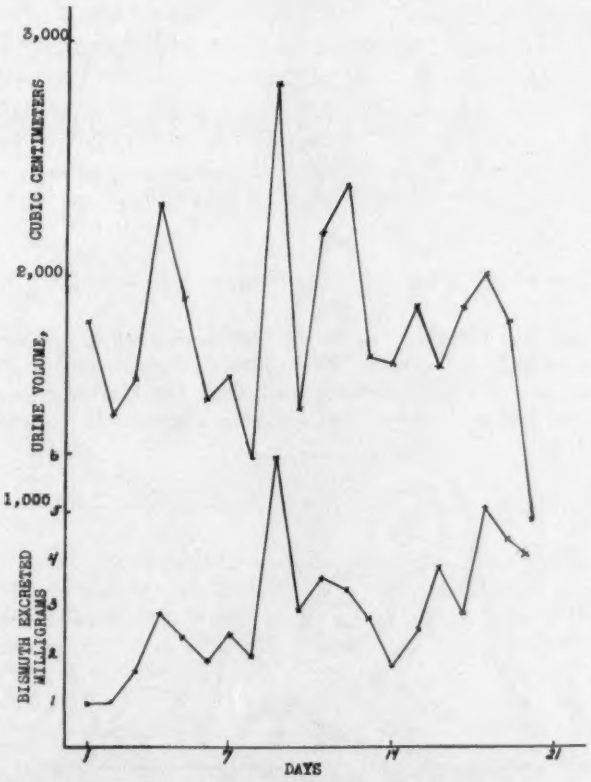


Chart 6 (case 6).—Within twenty days after the injection of 40 mg. of bismuth (1 cc. bismuth ethylcamphorate) each week for three weeks 48 per cent of the total bismuth injected was recovered in the urine. The average daily bismuth excretion was 1.8 mg. for the first week, 3.15 mg. for the second week and 3.72 mg. for the third week. The graph of the twenty-four hour urine volume is included to show that in some cases there is a tendency for the amount of bismuth excreted to follow in close relation to the volume of urine excreted.

injection, the average mean excretion being 29 per cent, regardless of dosage.

The average daily excretion of bismuth in urine usually varied directly with the dosage, after single injections and multiple injections.

In none of these patients was there evidence of nephrotoxic or other untoward effects.

SUMMARY

A study was made of the daily excretion of bismuth in the urine of 9 adult patients after the intramuscular administration of clinical doses of an oil-soluble bismuth compound (bismuth ethylcamphorate), each cubic centimeter of which contains 40 mg. of elemental bismuth.

Three patients had only single injections, receiving 40 mg., 80 mg. and 80 mg. of bismuth, respectively. Three patients received the 40

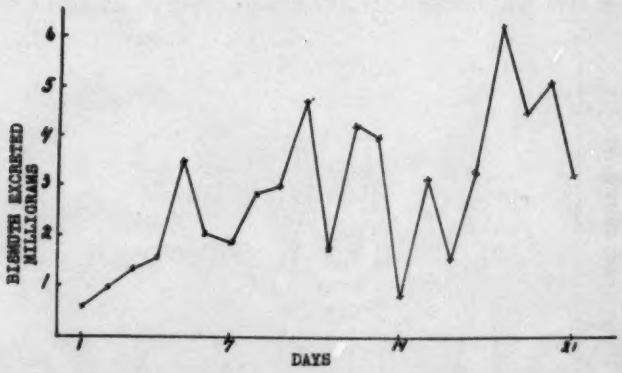


Chart 7 (case 7).—Injections of 80 mg. of bismuth (2 cc. bismuth ethylcamphorate) were made each week for three weeks, during which period 25 per cent of the injected bismuth was recovered in the urine. The average daily excretion of bismuth for the first week was 1.7 mg., for the second week 3.04 mg. and for the third week 3.9 mg.

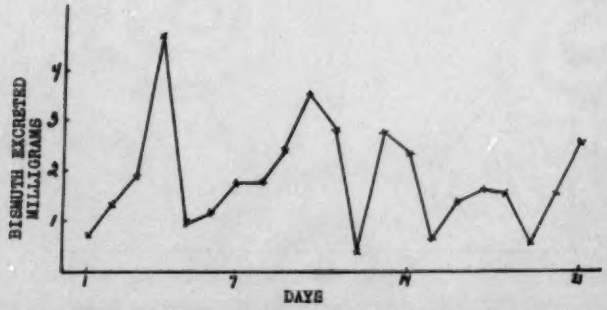


Chart 8 (case 8).—Injections of 80 mg. of bismuth (2 cc. bismuth ethylcamphorate) were made each week for three weeks, during which period 17 per cent of the bismuth was recovered in the urine. The average daily excretion for the first week was 1.84 mg., for the second week 2.31 mg. and for the third week 1.47 mg.

mg. dose per week for three weeks, while a second group of 3 patients received the 80 mg. dose per week for three weeks.

In the 3 cases in which single injections were given the daily average bismuth excretion per week showed a maximum during the first week, with decreasing levels thereafter, in 2 cases, while in 1 case the average bismuth excretion per week resulted practically in a straight line.

In the 6 cases of multiple injections the daily average bismuth excretion per week showed ascending levels for each successive week, the maximum average excretion being attained in the third week, in 4 cases. In the fifth case the average daily bismuth excretion showed practically a straight line, while in the sixth case there was an ascending level which attained maximum excretion through the second week and was followed by a slight decrease through the third week.

One patient received a single injection of 40 mg. of bismuth and excreted 36 per cent of this bismuth in the urine within eighteen days.

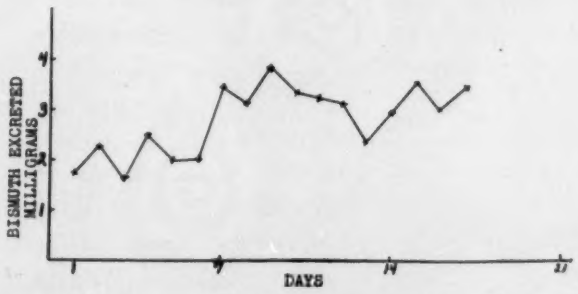


Chart 9 (case 9).—Injections of 80 mg. of bismuth (2 cc. bismuth ethylcamphorate) were given each week for three weeks; during the first eighteen days 26 per cent of the injected bismuth was recovered in the urine. The average daily bismuth excretion for the first week was 2.23 mg., for the second week 3.15 mg. and for the third week 3.4 mg.

Two patients each received single injections of 80 mg. of bismuth and excreted 29.5 and 20 per cent of this bismuth in the urine in eighteen and nineteen days, respectively.

Three patients received 40 mg. of bismuth each week for three weeks and excreted 48, 29 and 30 per cent of this bismuth in the urine in twenty, twenty-one and twenty-one days, respectively.

Three patients received 80 mg. of bismuth each week for three weeks and excreted 26, 25 and 17 per cent of this bismuth in the urine within eighteen, twenty-one and twenty-one days, respectively.

One patient received a single injection of 40 mg. of bismuth and had daily determinations of bismuth in the urine for eighteen days and thereafter at varying intervals until no further bismuth was excreted in the urine, the total observation period requiring seventy-three days.

Roentgenograms of the site of injection (gluteal muscle) at intervals varying from five hours to sixty days after the intramuscular administration of bismuth ethylcamphorate in all instances failed to show deposits of bismuth.

As judged by the average daily excretion of bismuth in the urine, the 2 cc. dose (80 mg.) of bismuth ethylcamphorate administered at seven day intervals is sufficient to maintain a sustained circulation of bismuth over a sufficient period of time to fall within the accepted standards of therapeutic effectiveness.

The fecal excretion of bismuth is not reported.

ACTION OF IODINE ON DISEASES OF THE SKIN AS INFLUENCED BY SEASON AND WEATHER

FREDERICK REHM SCHMIDT, M.D.

CHICAGO

The effect of the weather, climate and seasons on the incidence of cutaneous disease has recently been studied by Marchionini and Tor,[1] Walter [2] and myself.[3] Clinical observations of this character have been amplified and substantiated by Petersen and Milliken,[4] who have translated into terms of quantitative analysis the effect of fluctuations in barometric pressure, altitude and sunshine on the skin. These investigations have stimulated further study of the problem, with the purpose in mind of discovering the specific component in the environmental constellation that is responsible for the seasonal improvement noted in certain dermatoses.

In considering the effect of seasons and climate, dermatologists have realized that sunshine is not the only factor, for patients afflicted with atopic dermatitis or arthropathic psoriasis usually fare better in Arizona than in Florida. Beside such factors as the density of the air, humidity, pollens, fungi and temperature, there is the striking difference in altitudes between these two localities. At a medical meeting in Angora, Turkey, Fahri Izgi [5] stated that in his opinion the rarity of neurodermatitis occurring on the plateau of Central Anatolia may be attributed exclusively to the altitude.

From the Northwestern University Medical School and the Outpatient Department of Grant Hospital.

Read at the Sixty-Third Meeting of the American Dermatological Association, Inc., Colorado Springs, Colo., May 30, 1940.

1. Marchionini, A., and Tor, S.: Zur Klimatophysiologie und Pathologie der Haut, Arch. f. Dermat. u. Syph. **179**:421, 1939.

2. Walter, F., in Deliberationes Congressus dermatologorum internationalis IX-I Budapestini, Sept. 13-21, 1935, Leipzig, Johann Ambrosius Barth, 1935, vol. 1, p. 323.

3. Schmidt, F. R.: Skin Diseases and the Weather, Arch. Dermat. & Syph. **32**:781 (Nov.) 1935.

4. Petersen, W. F., and Milliken, M. E.: The Patient and the Weather, Ann Arbor, Mich., Edwards Brothers, Inc., 1934-1937, vols. 1-4.

5. Fahri Izgi: Spätexsudatives Ekzematoid Rost, Dermat. Wchnschr. **108**:639 (June 3) 1939.

The air at high altitudes is less dense and contains relatively less oxygen. Duerst [6] demonstrated that one way in which the body reacts to such an atmospheric environment is with stimulation of the thyroid gland. Increased amounts of thyroxine are released by the thyroid gland into the blood stream, from which a large portion is rapidly excreted in the urine and saliva. The fate of the residue of thyroxine will be considered later.

Not only does the average case of psoriasis show improvement at such altitudes, but it also shows improvement at lower altitudes during the summer months. The patient responds to both mountain and summer air with an increased production of thyroxine by the thyroid gland. Kendall and Simonsen [7] showed that the thyroid gland of an animal contains over twice as much iodine in July as in February. Veil and Sturm [8] demonstrated that a large part of this iodine is released in the blood stream, so that a higher iodine level is maintained in the blood in summer than in winter.

Any determination of the iodine content of the blood is open to criticism. A high level in the blood may merely indicate the passing of iodine from the thyroid gland on the way to its excretion in the urine or to its deposit in some tissue, where it will be stored until a metabolic demand is made on it.

A large portion of the iodine that is not excreted in the urine and saliva finds its way to the skin. Sturm and Buchholz [9] and Wehren [10] found that the skin and hair contain large amounts of iodine, of which some is constantly being withdrawn to satisfy its depletion elsewhere in the body. Another fraction is stored for future use, while the remainder is consumed in the process of tissue metabolism. Müller and von Fellenberg [11] showed that iodine is present in the skin in a biologically active form which is essential to the synthesis of protein.

The deduction that the content of cutaneous iodine also varies between summer and winter is inadmissible, for the data at hand pertain

---

6. Duerst, J. U.: Sauerstoffschwankungen der Atemluft in ihrer formbildenden Wirkung bei Mensch und Tier, Berne, Paul Haupt, 1937.

7. Kendall, E. C., and Simonsen, D. G.: Seasonal Variations in Iodine and Thyroxine Content of Thyroid Gland, J. Biol. Chem. **80**:357 (Dec.) 1928.

8. Veil, W. H., and Sturm, A.: Beiträge zur Kenntnis der Jodstoffwechsels, Deutsches Arch. f. klin. Med. **147**:166, 1925.

9. Sturm, A., and Buchholz, B.: Beiträge zur Kenntnis des Jodstoffwechsels, Deutsches Arch. f. klin. Med. **161**:227, 1928.

10. Wehren, E.: Ueber das Schicksal des Thyroxins in Organismus, Zurich, Leemann & Co., 1939.

11. Müller, C., and von Fellenberg, R.: Untersuchungen über das Schicksal des Thyroxins im Organismus, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **42**:661, 1932.

to the iodine content of skin obtained at autopsy. Sturm [12] pointed out that the microtitration of an amount of iodine less than 1 or 2 micrograms is difficult even when it is in solution; so the minute fraction of the element present in a small piece of skin has not been estimated.

A group of 74 patients with various chronic diseases of the skin were therefore subjected to iodine medication. The investigation extended over two years. Iodine was administered as the compound solution of iodine U. S. P. unless otherwise indicated. An average dose of 8 drops three times daily after meals was maintained until 1 to 2 ounces (30 to 60 cc.) had been taken. The blood pressure was recorded at each visit, but no surprising changes in the pressure were observed. There were no decided changes in the metabolic rate. No topical applications other than borated petrolatum were employed, and to this I attribute the fact that several patients failed to return for observation. No systemic or cutaneous symptoms of intolerance were found. Each case is selected as typical of a group of cases.

CASE 1.—A. W., a white man aged 28, presented himself in July 1938, with atopic dermatitis of ten years' duration. The condition of his skin was usually worse in hot, sultry weather. Scratch tests disclosed that his skin reacted strongly to dog's hair. When told of this the patient stated that he owned a dog at the time of onset of his cutaneous trouble but that he had not been near a dog since then. Attempts to desensitize him failed. He felt better after taking iodine in October, although the condition of his skin remained unchanged. The medication was repeated in July 1939, during a spell of hot, sultry weather. Itching soon grew more intense, and he stopped taking the medicine because the eruption began to spread over his body. There was slow improvement with a regimen of roentgen irradiation. Autohemotherapy failed to benefit the patient.

Four other patients with atopic dermatitis became visibly worse when iodine medication was instituted during hot, sultry weather. Each of these patients, however, had previously stated that such weather had always caused him great discomfort. Iodine was administered to the same patients in winter without exerting any visible influence other than producing slight subjective improvement in 3 of them. Five other persons with this disease did not respond clinically to iodine medication.

CASE 2.—A. W., a white woman aged 31, presented herself in 1934 with psoriasis of six years' duration. Topical applications and autohemotherapy had usually checked the spread of the eruption. The patient complained of frequent headaches. In December 1938 she was given iodine by mouth, without noticeable influence on the course of the disease. Returning in July 1939, during a spell of hot, sultry weather, she again took iodine. Seven days later she returned to say that she felt sick. She had a severe headache. The eruption had spread and pained her a great deal. Iodine medication was discontinued. A course of injections of whole blood seemed to arrest the progress of the disease. She soon felt much better. In March 1940 she returned to say that she had had the best winter for years. Her skin was comparatively clear.

12. Sturm, A.: Ein Beitrag zur Mikrojodtitration, Biochem. Ztschr. **200**:273, 1928.

CASE 3.—J. V., a white man aged 31, consulted me in May 1939, complaining of a widespread eruption and frequent headaches. A diagnosis of psoriasis was made. He had taken arsenic for the condition but had stopped doing so because it had made him sick. Autohemotherapy was employed, without benefit. In August, during a spell of hot, humid weather, treatment with a preparation containing 41 per cent of iodine combined with a fatty molecule was started. He took twelve tablets, returning to say that he "felt sick." The headaches had increased in intensity and frequency. Many red papules were distributed over the entire body. His accusation that the medicine had made him worse was unfortunately true.

CASE 4.—M. E., a white man aged 46, with psoriasis, had returned to me each winter for fourteen years for treatment which had never visibly benefited him. He again consulted me on Sept. 18, 1939. For years he had noticed that the eruption grew worse with the onset of cool weather. At such times his hands hurt a good deal. His fingers were painful. On this occasion the palms were dotted with numerous, discrete, scaly maculopapules. The nails showed changes typical of psoriasis. He took 30 tablets of iodine in lipoidal combination. He stated that the pain in his hands had stopped two days after he had started taking the tablets and that he felt much better generally. On examination the palms were soft and only a few lesions were present. He remained relatively free from psoriasis until January 1940, when a fresh crop of papules appeared. The same organic preparation of iodine was again taken but failed to halt the progress of the disease. Autohemotherapy was employed, and involution of the lesions was noticeable after three weeks of treatment.

CASE 5.—R. M., a 55 year old housewife, first visited the outpatient department of Grant Hospital in September 1939. She complained of a generalized eruption of twenty years' duration. A diagnosis of psoriasis was made. She stated that the rash always grew worse with the onset of cold weather. She felt chilly. At this season her hands hurt a good deal. She was given iodine. A week later she felt much better and warm again. Her "rheumatism" had disappeared. No new lesions had appeared. Whole blood therapy was started in December. One cubic centimeter of a preparation containing casein and sodium iodohydroxyquinoline sulfonate was added to the blood before it was injected into the gluteal muscles. In February 1940 she felt well, and the rash looked better to her than when she had used ointments. Involution of many lesions had occurred. The scalp, which had been covered with scales, was greatly improved.

CASE 6.—J. O., a white woman aged 24, consulted me on Sept. 24, 1939, for relief of psoriasis of ten years' duration. She had come to Chicago from Seattle, and the disease had steadily progressed throughout the summer. During the previous week she had suffered from headache, nausea and chilliness. The disease had lately appeared on the legs for the first time in her life. She was given iodine by mouth, returning three weeks later to say that she felt much better. The objective improvement was striking. Involution of most of the papules on the legs had occurred. No new lesions were observed. The older plaques on the back had cleared in the center. Autohemotherapy was employed in November, with considerable benefit.

These 5 cases were selected from a group of cases of psoriasis. An analysis of them shows that the patients usually responded unfavorably to the ingestion of iodine during hot, sultry weather in Chicago. At such times the entire level of iodine in the body is raised, necessitating

increased action of the adrenal gland in an attempt at compensation. The added increment of iodine at this season may suffice to upset the delicate mechanism of normal cornification.

The process of keratinization is intimately connected with the establishment of a proper balance between oxidation and reduction, for normal decomposition of the acid albumins of the nuclei cannot occur when the oxidation-reduction potential is disturbed. That this mechanism is of vital importance to the life of the skin has been established by Szent-Györgyi,[13] Lewis,[14] Radaeli [15] and others. I [16] found that the degree of oxidation varies in different parts of the skin, so that when iodine is taken up by the skin it is subjected to varying phases of oxidation and reduction.

The experiments of Müller and von Fellenberg [11] and numerous other investigators point to a close relation between iodine and the process of biologic oxidation. Shackell [17] showed that the internal administration of thyroxin and iodine increases tissue oxidation.

Just as endogenous iodine stimulates cutaneous oxidation, so the application of iodine to the skin likewise stimulates the gas metabolism of the skin. Sametinger [18] demonstrated that the rate of oxidation and the formation of carbon dioxide were both increased after the application of the tincture of iodine to a dog's skin. The absence of any appreciable redness or swelling of the painted area seems to exclude the presence of inflammation sufficient to cause such an acceleration of the gas metabolism in the skin.

The striking influence on the course of psoriasis when iodine was administered during the autumnal equinox is illustrated in cases 4 and 5. At such times iodine in the blood is starting to fall to its winter level, so that by late winter the body has lost a good deal of iodine. Iodine medication during this season may therefore supply a definite need and act as a catalyzer to stabilize cutaneous metabolism.

Many patients complained of frequent headaches and chilliness of the skin. Headache is regarded by many authorities as the most com-

---

13. Szent-Györgyi, A.: Mechanism of Biological Oxidation, Proc. Inst. Med. Chicago **12**:418 (Oct. 15) 1939.

14. Lewis, T.: Anatomy and Physiology of the Capillaries, New Haven, Conn., Yale University Press, 1929.

15. Radaeli, G.: Das Oxydations-Reduktions-Potentiale und die reduzierenden Prozesse in der lebendigen Haut, Arch. f. Dermat. u. Syph. **178**:253, 1938.

16. Schmidt, F. R.: Blood and Oxygen Supply of the Skin, Arch. Dermat. & Syph. **32**:576 (Oct.) 1935.

17. Shackell, L. F.: Biologic Assay of Thyroid, U. S. P., by Determination of the Oxygen Consumption in the Guinea Pig, J. Pharmacol. & Exper. Therap. **60**: 117, 1937.

18. Sametinger, E.: Die Wirkung von Jodtinktur auf den Sauerstoffverbrauch und auf die Durchblutung der Haut, Arch. f. exper. Path. u. Pharmakol. **159**:1, 1931.

mon clinical indicator of autonomic instability. It is of interest that it was in just such persons that iodine medication proved harmful during hot weather and beneficial at the equinox. These are persons who generally react to barometric fluctuations with headache (vasospasm) and disturbances of cutaneous sensation. These autonomically unstable persons are poorly buffered chemically in respect to calcium, phosphorus, chlorides and iodine. The reaction of the tissues easily becomes acid, and iodine is lost from the body during such periods of meteorologic unrest as the autumnal and the vernal equinox in Chicago.

Case 6 illustrates the possible fate of a psoriatic patient transferred from a favorable climate to one relatively unfavorable. The extent to which such a person reacts to environmental change is also conditioned by his state of autonomic stability. His degree of adjustment to climatic disturbances is thus strictly limited.

From these studies it appears that iodine is best administered to patients with psoriasis in spring and fall, at a time when the body is starting to lose iodine and electrolytes, such as calcium and phosphorus. Its administration during hot, sultry weather was found harmful. In winter it was without visible effect. Injections of whole blood during summer and winter, as a form of "interval" treatment, generally proved efficacious in arresting the progress of the disease. Cases 2, 4, 5 and 6 illustrate this point.

Several theories may be advanced to explain the action of autohemotherapy in psoriasis. The physiologic process of cornification is dependent on, among other factors, the normal fermentation of enzymes in conjunction with an undisturbed glycogen metabolism. The evidence at hand points to the assumption that the formation of such enzymes as tyrosinase and reductase is controlled by the autonomic nervous system. Numerous investigators have shown that nonspecific, alterative treatment, such as autohemotherapy, stimulates the autonomic nervous system. In this way the abnormal sequence of events leading to parakeratosis may be halted and order be restored, with normal keratinization as the result.

The second prerequisite for abnormal keratinization is a disturbance of glycogen metabolism. It has been known for a long time that the administration of iodine leads to mobilization of hepatic glycogen, thus increasing the supply of glycogen available for cellular synthesis.

Another way in which whole blood therapy may bring about involution of psoriasis is by altering the hydrogen ion concentration of the skin. Dziulikowska [19] recently demonstrated that nonspecific treatment of this character induces phases of cutaneous alkalinity. In winter the

19. Dziulikowska, C.: Ueber den Einfluss der physikalischen und chemischen Reize auf die Wasserstoffionenkonzentration der Haut, Arch. f. Dermat. u. Syph. **178**:673, 1939.

body tissues grow increasingly more acid with the approach of spring, owing to longer and more frequent periods of spasm and anoxemia that are caused, to a large extent, by meteorologic unrest. Autohemotherapy may thus act to reduce this acidity.

The specific manner in which alkalinity apparently stops parakeratosis may lie in the restoration of an optimal environment for the process of fermentation. The precept of Unna to treat patients with psoriasis with alkaline remedies finds support in the experiments of Wense,[20] who observed that the enzymatic action of such a ferment as tyrosinase is carried on best at a p_H of 7.6 to 8.

Swartz [21] obtained cures in 2 of 8 patients with psoriasis treated with inhalations of ethyl iodide. My results were not so favorable, for I do not recall a single cure obtained with iodine medication in this series of cases. The dosage or the form in which the iodine was administered may have been inadequate. I am now using thyroxin in tablet form and believe that the results are better. Müller and von Fellenberg [11] observed that potassium iodide is neither stored in the skin nor chemically bound to protein to the extent that thyroxin is.

The administration of an iodide combined with a fatty molecule, such as brassidic acid, to some patients was done for two reasons. Loeb and Velden [22] showed that this preparation exerts great lipotropic action, which seemed important in the treatment of psoriasis. Secondly, a patient can thus be maintained for a longer time under the influence of iodine, because its elimination is slower than that of the alkaline iodides.

Case 7.—M. K., a white woman aged 32, presented herself at the Northwestern University Medical School in March 1939, complaining of loss of hair over the entire body. Hair first fell out in patches on the scalp in the third month of pregnancy in April 1938, and by October complete loss of hair had occurred. She had frequent headaches. Slight exophthalmos was present. The basal metabolic rate was plus 12 per cent. The scalp was sensitive to touch. The patient had received ultraviolet irradiation, without benefit. She was given iodine by mouth. On July 14, 1939, after having taken 2 ounces (60 cc.) of compound solution of iodine U. S. P., she stated that she felt much better. The scalp was not sensitive to touch. Hair was starting to grow in patches. By October she was able to discard her wig, because hair was appearing over the entire scalp. In February 1940 she felt well, and there were no areas of alopecia.

The pathogenesis of alopecia areata is intimately connected with spasm of the terminal blood vessel of the hair papilla. As evidence of the danger to which the vitality of the hair is subjected by such spasm

20. Wense, T.: Ueber die Wirkung des Acetaldehydes auf die Haut, Arch. f. Dermat. u. Syph. **179**:136, 1939.

21. Swartz, J. H.: Treatment of Fungous Infections with Ethyl Iodide Inhalations, Arch. Dermat. & Syph. **40**:962 (Dec.) 1939.

22. Loeb, O., and Velden, R.: Ueber die Grundlagen der internen Therapie mit Jodfettsaurederivaten, Therap. Monatsh. **25**:209, 1911.

and anoxemia, Lévy-Franckel and Cailliau [23] pointed to the diminished number of capillaries in areas of alopecia areata. They also stressed the frequency with which such loss of hair is associated with diseases in which the autonomic nervous system is involved, for example, exophthalmic goiter, scleroderma and vitiligo.

Petersen demonstrated that the vasospasm present in this disease can be induced by sudden changes in the barometric pressure. The spasm, with its attendant anoxemia, following in the wake of a rapid drop in temperature, may be of short or long duration, thus explaining the numerous clinical variants. Any agent that helps prevent or overcome spasm may be assumed to restore the normal mechanism of biologic oxidation. Such an agent is iodine. Guggenheimer and Fisher [24] showed that iodine, even in minimal doses, causes demonstrable vasodilatation of the peripheral blood vessels.

Considerable experimental data have accumulated to support the clinical observation that the growth of hair is influenced by seasonal, climatic and meteorologic factors. As previously stated, a large residue of the iodine released by the thyroid gland is ultimately stored in the hair. The presence of such relatively large amounts of iodine in the hair of animals which are producing great amounts of thyroxine under the stress of meteorologic unrest may explain the fact that hair grows faster in such animals.

Goldsmith [25] obtained good results with iodine medication in persons suffering from senile pruritus. Alleviation of itching in this condition may be attributed in a similar manner to improved tissue oxidation induced by vasodilatation. Substantiation for this hypothesis may be found in my observation in this series of cases that patients with senile pruritus associated with arteriosclerosis did better on iodine medication than those in whom no hardening of the vessels was detected clinically.

SUMMARY AND CONCLUSIONS

Iodine was administered to 74 patients suffering from various diseases of the skin uncomplicated by infection with fungi.

Psoriasis, alopecia areata and certain forms of pruritus were found especially responsive to iodine.

The type of reaction to iodine medication in one and the same person varied at different seasons.

---

23. Lévy-Franckel, A., and Cailliau, F.: Recherches sur le mécanisme physiopathologique de la pelade, Ann. de dermat. et syph. **6**:391 (May) 1935.

24. Guggenheimer, H., and Fisher, I. L.: Die Wirkung des Jods auf Herz und Gefäss-system, Ztschr. f. d. ges. exper. Med. **58**:196, 1927; Med. Klin. **23**:385 (March 18) 1927.

25. Goldsmith, W. N.: The Significance and Treatment of Itching, Practitioner **142**:36 (Jan.) 1939.

The degree of this reaction appeared to be conditioned by the relative stability of the person's autonomic nervous system. Patients possessing an unstable autonomic system reacted excessively to the administration of iodine.

Seasonal, meteorologic and climatic factors apparently determine the action of iodine on the course of cutaneous disease.

It is hoped that this investigation will stimulate further work in this field.

ABSTRACT OF DISCUSSION

DR. M. F. ENGMAN JR., St. Louis: This paper is an approach to a fundamental problem that has been given little attention in the past, and I hope that it will stimulate more work along the same line.

I believe that all physicians have noticed that changes in barometric pressure, temperature and seasons have a profound effect on disease. There are certainly days and weeks in which a particular disease will be worse or better. I think this is particularly true of eczema and neurodermatitis (atopic dermatitis). As an example of the effect of seasonal and environmental changes affecting chronic diseases, I offer acne vulgaris. During the summer acne usually clears up. Then in the fall the acne begins to get worse, and I think the peak of severity is reached some time around Christmas.

CUTIS VERTICIS GYRATA AND ACROMEGALY

ERWIN P. ZEISLER, M.D.
CHICAGO
AND
LESTER M. WIEDER, M.D.
MILWAUKEE

The morphologic changes in the scalp which characterize cutis verticis gyrata were first described by Robert [1] in 1848 and by McDowell [2] and Cowan [3] in 1893 in microcephalic idiots. It was not until 1906 that Jadassohn [4] called to the attention of dermatologists the condition which in the following year was given its present name of cutis verticis gyrata by Unna.[5]

During the ensuing twenty-five years Stratton [6] found that 158 cases of this condition had been reported by European physicians. Many of the earlier observers, basing their opinions on clinical and histologic studies in single cases, concluded that the condition was due to postinflammatory changes, nevoid infiltrates and tumors, depending on the type of change met within their personal experiences. This confusion led Fischer [7] to attempt to classify the condition according to its causes, and his classification has generally been accepted as a workable one by subsequent observers.

Fischer stated the belief that true cutis verticis gyrata occurs as a developmental anomaly, probably atavistic in type, representing a reversion to a lower form of life in which the muscles of the scalp could move it at will. This is probably the type originally described as present in microcephalic idiots, but a definite statement cannot be made without knowledge of the pituitary status, as determined by modern diagnostic study. For examples of the atavistic type, one might quote Charles Darwin, who described an arrangement of the skin of the scalp and even of the face in primitive African and Melanesian tribes which corresponds to later clinical descriptions of cutis verticis gyrata and closely

---

Read at the Sixty-Third Meeting of the American Dermatological Association, Inc., Colorado Springs, Colo., June 1, 1940.

1. Robert: J. de chir. **1**:125, 1848.
2. McDowell, T. W.: J. Ment. Sc. **34**:62, 1893.
3. Cowan, J. J.: J. Ment. Sc. **34**:539, 1893.
4. Jadassohn, J.: Verhandl. d. deutsch. dermat. Gesellsch. **9**:451, 1906.
5. Unna, P.: Monatsh. f. prakt. Dermat. **14**:227, 1907.
6. Stratton, E. K.: Cutis Verticis Gyrata: Report of a Case, Arch. Dermat. & Syph. **27**:392 (March) 1933.
7. Fischer, J.: Arch. f. Dermat. u. Syph. **141**:251, 1922.

simulates the furrowed skins of certain lower animals. Fischer regarded the conditions in all other cases as being diseases of the scalp "in the form of cutis verticis gyrata" and classified them as to their causation, as determined by histologic study, for instance, as (*1*) inflammatory diseases, acute or chronic, (*2*) anomalous and apparently congenital hypertrophies of the connective tissue, (*3*) tumors, such as cerebriform nevi and neurofibromas, and (*4*) changes in the scalp occasioned by proliferation of tissue in systemic diseases, such as myxedema, acromegaly, leukemia and cretinism.

Although cases of cutis verticis gyrata in association with acromegaly had been observed and described in the literature, including that of America, or presented before medical societies previously, Weber [8] in 1928 stressed the relation in an article and tabulated 12 cases which had been studied by other observers. This author concluded that the excessive thickening of the connective tissue of the skin, which is not only too thick but too large for the skull, produces the characteristic gyri. Subsequently this association received more attention, especially in the Scandinavian literature, as the result of studies by Renander [9] and Grönberg.[10] The latter stressed the leonine aspect of the forehead in his patient, suggesting leprosy, and the hypertrophy of the hands and feet, as well as other clinical and roentgenologic evidences indicating an endocrine dysfunction closely akin to acromegaly, and gave the syndrome the title "megalia (hyperplasia) cutis et osseum." To the best of our knowledge, the cases herein reported constitute the third and fourth cases of cutis verticis gyrata associated with pituitary disease in the American literature, the first having been reported by Sisson [11] and the second by Cushing and Davidoff,[12] who gave the disorder the title "bulldog scalp." It is significant that brain surgeons occasionally have encountered this anomaly of the scalp accidentally in the course of operations on the pituitary gland. Also, many competent internists and endocrinologists are unaware that this condition is an important diagnostic clue to an underlying endocrine disturbance, without other outward prominent evidence of the disease, as illustrated in the account of case 2. These facts have stimulated the preparation of this clinical report.

---

8. Weber, F. P.: Brit. J. Dermat. **40**:1, 1928.

9. Renander, A.: Acta med. Scandinav. **67**:24, 1927; **96**:186, 1938; Acta radiol. **9**:399, 1928; **18**:653, 1937; **19**:254, 1938.

10. Grönberg, A.: Acta med. Scandinav. **67**:24, 1927.

11. Sisson, R. J.: Cutis Verticis Gyrata, J. A. M. A. **86**:1126 (April 10) 1926.

12. Cushing, H., and Davidoff, L. M.: The Pathological Findings in Four Autopsied Cases of Acromegaly, Monograph 22, Rockefeller Institute for Medical Research, 1927, p. 31, fig. 26. Case of c. v. g. presented as "bull-dog scalp" in an acromegalic person.

It is not our purpose to present here in great detail a review of the earlier literature of the cases in which the condition was due to causes other than pituitary disturbances. This has been well done in the American literature by Stratton,[6] Madden [13] and Hammond and Ransom,[14] who presented 2 cases of the inflammatory type. Madden emphasized the fact that the structure of the scalp favors the formation of folds and that abnormal collections of cells, whatever their origin or type, may result in an apparently identical morphologic end result. Hammond and Ransom, in a careful histologic and clinical report of 2 cases of cerebriform nevi of the scalp, stressed the fact that this condition is distinctly different from all other types of cutis verticis gyrata. It is apparent, therefore, that instead of being satisfied with the clinical-morphologic diagnosis, each case must be studied carefully in an attempt to arrive at a diagnosis based on causation.

There is probably no cutaneous disease which lends itself more readily to immediate clinical diagnosis than cutis verticis gyrata. However, this diagnosis should serve only as a provisional working diagnosis on which further intensive study of the case should be based. An accurate history of the circumstances of the onset of the condition may be of value, especially in cases in which the condition is apparently a sequela of trauma, infection (local) or inflammatory disease; in this group the gyri are apt to be less regular in outline and distribution and show evidence of follicular changes, as compared with those in cases in which the condition is due to systemic factors. In dissecting folliculitis of the scalp (perifolliculitis capitis abscedens et suffodiens), the appearance of the scalp may after healing present scarring, with the nodules and folds resembling the convolutions of the brain. A history of development of the condition early in life suggests the possibility of nevoid or anomalous developmental etiology, but even in this type of case both study of the local tissue and roentgenographic study of the skull, with special reference to the sellar region, should be carried out.

In all cases in which the cause is not apparent, a biopsy should be performed first as a possible means of detecting specific types of infiltrating tissue, such as leukemia, nevus, tumor and inflammatory cellular elements. When such study fails to indicate the etiologic diagnosis, even in the absence of other gross outward clinical signs, the case should be thoroughly investigated for endocrine disease, including myxedema, as well as for pituitary disease involving the anterior lobe. As part of such examination roentgenograms of the skull and of the extremities play an important part. Other important laboratory studies include the basal metabolic test, careful examinations of urine, the test for

13. Madden, J.: Minnesota Med. **18**:536, 1936.

14. Hammond, G., and Ransom, H. K.: Cerebriform Nevus Resembling Cutis Verticis Gyrata, Arch. Surg. **35**:309 (Aug.) 1937.

diminished sensitiveness to epinephrine and the sugar tolerance test. In the event of failure to identify a definite etiologic factor after thorough investigation, the patient should be kept under observation with periodic reexamination, including repeated roentgen ray examination of the skull, measurement of visual acuity and fields and examination of the urine. It is noteworthy that in both the cases presented here there was evidence of serious metabolic disturbances, although in the second case a relation between the pituitary disease and the metabolic changes ultimately responsible for the patient's death could not be established.

The 2 following case reports well illustrate the association of cutis verticis gyrata as a readily detected clinical sign of pituitary disease of the acromegalic type.

REPORT OF CASES

CASE 1.—R. S., a white man aged 44, has been under observation for the past fifteen years with known symptoms of acromegaly. He has had diabetes for five years and urinary incontinence for four years. He has been admitted to the hospital at various times in the last four years on account of pain in the lower part of the back and in the legs, which was diagnosed as sacroiliac arthritis, and sciatica and kyphoscoliosis associated with acromegaly in 1935. In 1937 he was admitted to the hospital with polyuria, polydipsia, loss of weight and muscular weakness of two months' duration. The concentration of sugar in his blood at that time varied from 205 to 230 mg. per hundred cubic centimeters, and his diabetic symptoms were controlled with insulin and diet. In November 1938 he was again admitted on account of pain in the lumbosacral region, for which a laminectomy was performed and from which he made a good recovery. The neurologic examination revealed the following picture: slight bilateral pes cavus; moderate atrophy of all muscular groups of both lower extremities and buttocks; good motor power in the lower extremities, and absence of knee jerks even on reenforcement. The sensory examination showed a saddle-shaped area of analgesia and anesthesia (third, fourth and fifth sacral vertebrae); intact deep sensibility; a band of hyperalgesia anteriorly and posteriorly, just above the iliac crest and extending around the groin and abdomen; loss of sensation of the genitalia, and intact abdominal reflexes bilaterally. Power in the upper extremities was good, but the reflexes were obtained only with reenforcement. The cranial nerves were normal, and the ocular fundi appeared normal. A grossly tested visual field on the left seemed constricted.

Roentgenograms of the spine showed an old osteoarthritic process mainly of the fourth and fifth lumbar vertebrae. The chemical examination of the blood revealed: uric acid 6.6 mg., calcium 12 mg., phosphorus 4 mg., nonprotein nitrogen 33 mg., phosphates 3.2 units and sugar 160 to 260 mg. per hundred cubic centimeters. The blood count showed no abnormality, and the Wassermann and Kahn reactions were negative on repeated examinations. The patient was intelligent and alert, although he walked with some difficulty.

The condition of the scalp had been present for some years, having developed about the same time that the enlargement of his hands and the changes in his facies were noted. After the hair on the scalp was shaved, the entire scalp was found to present deep anteroposterior convolutions, roughly resembling those of the cerebral hemispheres. The forehead also presented deep transverse folds. In

addition to this, physical examination showed striking evidence of an advanced degree of acromegaly. There was general enlargement of the head, thickening of the nose and lips, slight exophthalmos, decided prognathism and enlargement and prominence of the ears. A thickened glabella and prominent malar eminences gave the patient a leonine expression. The teeth were widely spaced, and the palate was high arched. The tongue was rather large, and there were many nevi on the face and trunk. The skin of the face was doughy and inelastic, resembling that in cases of myxedema, and showed an excessive sebaceous secretion. The hair on the scalp was coarse and abundant and concealed the furrows almost

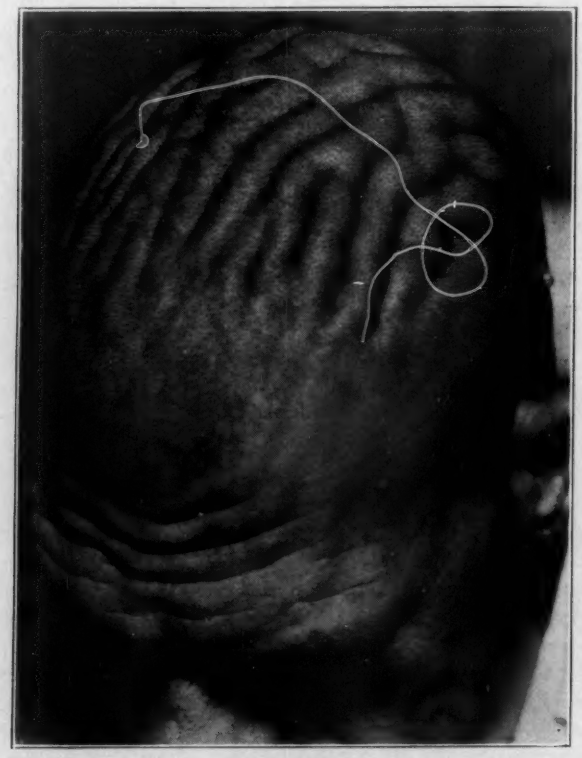


Fig. 1 (case 1).—Furrows and folds of the scalp and forehead in a patient with advanced acromegaly (Dr. Zeisler).

completely. The chest was barrel shaped and emphysematous. There was kyphoscoliosis of the lower thoracic and lumbar vertebrae, with a protuberance at the lumbosacral junction. The soft parts of the hands were enormously thickened, presenting the characteristic "spade" type of deformity, with sausage-shaped fingers with clubbed ends, thickened skin and localized hyperhidrosis. The feet showed similar changes. The results of physical examination were interpreted as those of advanced acromegaly due to an eosinophilic adenoma of the pituitary, associated with diabetes, osteoarthritis of the vertebral joints and cutis verticis gyrata.

Roentgenograms of the skull showed definite enlargement of the accessory sinuses, particularly the frontal, which extended upward to a point almost midway

between the nasion and the vertex. The bones of the calvarium were unusually thick. There was a high degree of calcification of the pineal gland and choroid plexus. There was decided destruction of the structures in the region of the sella turcica, with loss of the floor and posterior clinoid process. The changes were considered typical of those seen in cases of acromegaly.

The bones of the hands were large and the phalanges wide in proportion to their length. There were considerable tufting of the terminal phalanges and hypertrophy of their bases. While these changes are sometimes seen in normal persons, they are more commonly observed in acromegalic ones. It was concluded that the roentgenographic changes confirmed the clinical diagnosis, namely, that the patient was suffering from a pituitary tumor, with acromegalic changes.

Case 2.—J. W., a Negro aged 35, was referred to the department of dermatology and syphilology of the Milwaukee County Hospital on Aug. 13, 1929, with

Fig. 2 (case 1).—Roentgenogram of the skull showing enlarged accessory sinuses, thickening of the bones of the calvarium, calcification of the pineal gland and choroid plexus and severe destruction of the structures in the region of the sella turcica, with loss of the floor and posterior clinoid processes.

a provisional diagnosis of cerebrospinal syphilis, which was based on the patient's history that he had been treated for this condition previously in clinics in other cities. Further questioning revealed that his chief complaints were persistent fronto-occipital headache and progressive impairment of vision for ten or twelve years, especially in the left eye, with occasional transient diplopia. There was no history of other symptoms of any description, and he did not recall ever having had lesions suggestive of early syphilis. However, at one of the clinics he had been told that his Wassermann reaction was positive and had received considerable antisyphilitic treatment, without appreciable effect on his symptoms. Questioned as to the duration of the condition of the scalp, the patient stated that it had begun at about the same time the headache and visual symptoms were first noted

and that progression of the symptoms and the changes in the scalp had been of about the same degree. At no time had there been any inflammatory change in the scalp, and he was certain that until twelve or fourteen years preceding his entrance to the hospital his scalp had been perfectly smooth. This statement was corroborated by the patient's wife.

Examination showed the patient to be well nourished but not obese. Mentally he was alert and intelligent, and no evidence of mental aberration could be detected from his conversation. The scalp presented alternate deep furrows and ridges arranged in a gyrate and anteroposterior linear manner and involving the entire

Fig. 3 (case 1).—Roentgenographic changes in the hands, showing enormous enlargement of the bones and soft parts, tufting of the terminal phalanges and hypertrophy of their bases.

vertex, frontal, parietal and occipital portions of the scalp. The furrows felt rather tightly bound down to the underlying structures, but the ridges were soft and easily movable. The bony landmarks of the face were prominent but not to a greater degree than may occasionally be exhibited by the normal Negro. The skin of the face, especially of the forehead, showed deep wrinkles somewhat suggestive of an earlier stage of the condition present in the scalp. The neurologic examination showed only slight sluggishness of the pupillary reaction to light and weakness of the left external ocular rectus muscle. The tendon reflexes, gait and station

were normal. The extremities were not visibly enlarged. He had no difficulty in wearing gloves or shoes that he had formerly worn. The secondary sex characteristics were normal.

Examination of the eyegrounds showed the retina of the right eye to be pale, and the eyegrounds of the left could not be seen at all owing to active choroiditis; there was practically no vision in the left eye. The visual fields examined subsequently were moderately contracted in the right eye and greatly contracted in the left.

Wassermann reactions of the blood were repeatedly negative. The spinal fluid was normal.

Roentgenograms of the skull showed the bones of the vault to be thick, even for a Negro, with large accessory sinuses and prominent superior maxillas. There was decided thinning of the posterior clinoids, and the anterior clinoid on the left was apparently eroded, with erosion of the floor of the left side into the sphenoid

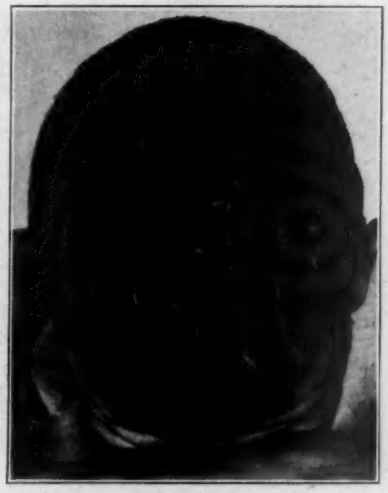


Fig. 4 (case 2).—Anteroposterior folds over the frontal part of the scalp (Dr. Wieder).

sinus. The metacarpal bones were short and thick. The tubercles of the distal phalanges were particularly prominent, and there were projections extending outward from the bases of the distal phalanges.

During a short period of hospitalization for further study the temperature was continuously normal. The blood pressure averaged 155 systolic and 100 diastolic. The urine showed no sugar at any time. The dextrose tolerance curve was normal. The basal metabolic rate was + 12 per cent. The blood count and the results of chemical examination of the blood were essentially normal (nonprotein nitrogen 37.3 mg., urea nitrogen 27.5 mg., creatinine 1.6 mg. and cholesterol 0.133 mg. per hundred cubic centimeters; sugar 0.8 and sodium chloride 0.462 per cent).

A biopsy was performed. A piece of tissue extending from the crest of a ridge in the vertex to the base of the adjoining furrow was excised. It was cut in a plane transverse to the long axis of the gyrus from which the section was taken, thus enabling comparative study of the hypertrophic center of the gyrus as well as its lateral, bound-down margin. The epidermis showed no remarkable changes.

In the corium the glandular elements and the hair follicles appeared to be unusually well developed, although without definite abnormality. No inflammatory changes were found. The most noticeable deviation from the normal lay in the increased number of the collagen bundles and the intensity of staining in them, especially in the upper half of the corium in the portion of the section corresponding to the crest of the gyrus examined. Although definite formations of fibrous bands could not be identified, the general architecture of the sections was interpreted as being compatible with the theory advanced by Stratton to account for the production of ridges and furrows in cutis verticis gyrata, namely, that there may be an inherent tendency for some types of tissue to grow faster than others and that such overgrowth between the dense normal fibrous bands binding the scalp to the pericranium would cause an arrangement of folds, the hypertrophy being chiefly found in the collagen bundles in the case under discussion and in the nevus cells and leukocytes in the various other conditions resembling cutis verticis gyrata.

Fig. 5 (case 2).—Roentgenogram showing moderately enlarged sella turcica, with thinning of the clinoid processes.

In addition to the theory which may account for the mechanism of the development of folds in cutis verticis gyrata of acromegalic origin, other explanations must be sought for the occasional case in which the condition is unilateral. Weber [15] cited such a case and stated the belief that in certain persons there exists a difference in "local soil" of corresponding parts of the body, so that a "general agent"—such as a pathologically altered endocrine secretion—exerts a greater effect on one organ than on another and even more on one side of the body than on the corresponding opposite part. No basic explanation of this phenomenon is given.

15. Weber, F. P., and Atkinson, F. R. B.: Brit. J. Dermat. **40**:454, 1928.

On the basis of the clinical symptoms, observations on the eyes and the bony changes exhibited in the roentgenograms, a diagnosis of probable eosinophilic tumor of the pituitary gland was made.

The patient was kept under intermittent observation until his death in June 1938. The only therapy of note consisted of a short course of roentgen ray treatments directed to the area of the pituitary in 1931 and 1932; these produced no definite effect on subsequent symptoms, and no remarkable changes were noted in the appearance of the structure of the skull on repeated roentgen ray examination during the succeeding six or seven years.

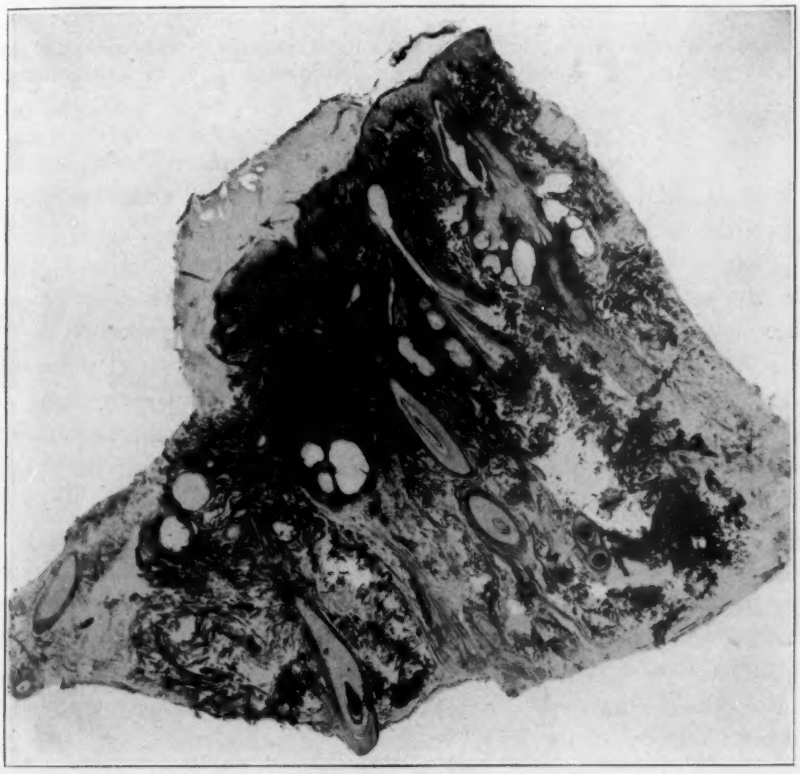


Fig. 6 (case 2).—Photomicrograph (Van Gieson stain, × 19) showing hypertrophy of the connective tissue in gyrus cut transversely and increased number and intensified staining of the collagen bundles in the upper half of the corium.

The patient continued to suffer from severe headaches, chiefly occipital, and the vision was practically unchanged. In October 1937, in the course of a routine check-up re-examination, his blood pressure was found to be 170 systolic and 90 diastolic, and the urine showed numerous hyaline casts and much albumin. His subsequent clinical course during the succeeding eight months was progressively downhill, the patient dying on June 7, 1938, of malignant hypertension with degenerative cardiorenal changes.

The autopsy showed the sella turcica to be widened posteriorly and laterally, measuring 2 cm. anteroposteriorly and 2 cm. laterally. The posterior clinoid

processes were flattened, and the presence or absence of erosion was not noted. The pituitary gland was found to be cystic and enlarged to such an extent that it was difficult to determine the architecture on gross cut sections. On microscopic examination, the capsule was found to be thickened owing to excessive fibrosis. On the surface and occasionally within the body of the gland nests of monocytes and multinucleated cells were found embedded within the connective tissue. The tubular structure of the gland was distorted. The predominating cells were large eosinophils which stained a deep pinkish red with the ordinary hemotoxylin-eosin stain. The remaining cells present were few in number. The pars intermedia was occupied by several small cysts containing a colloid-like material. The posterior lobe showed no unusual changes. The microscopic picture was considered compatible with that of chromophilic adenoma of the eosinophilic type, according to the classification of Dott, Bailey and Cushing,[16] which accompanies the hyperpituitary syndrome.

COMMENT

Investigation of the literature together with the 2 additional cases presented here indicates that cutis verticis gyrata may be added to the various other clinical signs pointing to pituitary disease. That it may be almost the only external sign and overlooked as such is shown by the clinical account of case 2. Although only a small proportion of all cases of acromegaly exhibit this finding, it is probable that of the many cases described in the literature, more may have been early signs of oncoming pituitary disease than were recognized as such. Because of this probability, we wish to reemphasize the need for careful study, with the inclusion of routine roentgenographic examination of the skill and extremities in this group of cases. We also wish to emphasize that the finding of a sella normal in size on roentgen ray examination does not necessarily negate the diagnosis of associated cutis verticis gyrata with acromegaly, as illustrated by Sisson's case, which, although one of frank acromegaly, showed a sella of apparently normal size. In some cases a final diagnosis can be established only after prolonged study and repeated reexamination.

Because of the scant attention this subject has been given in the American literature, it is our object to bring our 2 cases of cutis verticis gyrata associated with acromegaly to the attention of other physicians, especially dermatologists, as the latter may be the first to see the patient, and prompt recognition of the significance of the condition may bring about the detection of a serious underlying disease.

Dr. S. A. Morton, Columbia Hospital, Milwaukee, interpreted the roentgenograms, and Dr. John Grill, Milwaukee County Hospital, Wauwatosa, Wis., supplied the details of the results of autopsy in case 2.

16. Dott, N. M.; Bailey, P., and Cushing, H.: Brit. J. Surg. **13**:314, 1925.

ABSTRACT OF DISCUSSION

DR. FRED D. WEIDMAN, Philadelphia: I have recently had the occasion to study histologically 5 cases of cutis verticis gyrata, the specimens from all of which came from a state institution for persons with epilepsy, through Dr. Thomas Butterworth. In none of these were there any symptoms of acromegaly. No nervous disease other than epilepsy could be established in the cases.

I think that it is rather generally granted that cutis verticis gyrata is only a clinical entity. It is doubtlessly not an etiologic entity any more than zoster is.

Curiosity naturally centers on what the anatomic explanation for the folds may be. In the histologic studies of the abundant material from the institution, some valuable information came to light. It was emphasized to the surgeon who obtained the biopsy specimens that it was necessary to get the full extent of a convolution, with the sulcus on each side. The result was that some of the slabs of tissue were an inch or two (2.5 to 5 cm.) in length, in fact so long that celloidin (pyroxylin) was employed for embedding. This gave a splendid opportunity for comparing the composition of the different levels of the skin over a long stretch.

One idea as to the reason for these convolutions is that there are fibrous septums extending from the epidermis to the periosteum underneath, that they bind the skin more closely at those points—comparable to Cooper's ligaments in the breast, which are responsible for the pigskin markings in mammary cancer—and that there are increases of fibrous tissue between these points of attachment which cause a bulging of the skin (convolution) of the scalp. Such phenomena did not appear in any of my sections. What little increase in tissue there was in the bulges appeared to be due to fat.

In my sections, the factor that seemed to be the more responsible for the bulge was the hair shafts. I noted that Dr. Zeisler remarked in his first case that the hairs were numerous and were robust, and I think that it is probably a matter of common clinical observation in epileptics that the hair is commonly robust and closely placed. From the preliminary study of my sections, too, it would appear that the hair shafts are both more robust and more closely placed than they are in normal scalps. In addition, a good sized slab of this scalp tissue —for example, ⅛ or ¼ inch (0.3 or 0.6 cm.) thick and 2 inches (5 cm.) long—was cleared by the wintergreen oil technic (Spalteholz). The skin became so transparent that the individual hair shafts (black) stood out. By transmitted light, on examining with the naked eye, one could then recognize the abundance of the hair shafts.

After this, it is logical to try to reconcile this abnormal growth of hair with endocrine, nervous conditions, in which the pituitary comes under consideration at once. In short, at least tentatively, it is permissible to regard the growth processes of hair, whether initiated by pituitarism or not, as the possible explanation of the increased bulk of tissue in the scalp. With this increased bulk the scalp buckles and results in convolutions.

DR. ERWIN P. ZEISLER, Chicago: I hope that none of the American dermatologists will feel particularly slighted because their names were not mentioned in this article. Dr. Wise, I think, recorded the first American case of this condition; Dr. Oliver also reported a case some time ago, and there have been several others. But most of these reports were clinical descriptions of the disease, and no cause was recorded. I think in 1 case syphilis was mentioned as a possible etiologic factor. In fact, in many of the earlier descriptions of the disease it was stated that the condition may be simply a developmental anomaly or a nevus.

I have not said anything about the possible treatment of this condition. It is obvious that nothing can be done for it except in the cerebriform nevi. Such lesions have been removed surgically, with subsequent plastic procedure and good cosmetic results.

I think that in many of the cases in which the condition was recorded as due to inflammatory changes and trauma the presenters have failed to recognize the possible endocrine basis. Cases are reported in which the condition is called impetigo or psoriasis of the scalp followed by cutis verticis gyrata. It is nonsense to suppose that a simple inflammatory change without some serious metabolic disturbance could produce gyri and furrows that look like cerebral hemispheres. I think that the same argument applies against trauma as a cause.

I suspect that in the future all dermatologists will probably make more careful studies with reference to the pituitary cause of this disease.

PITYRIASIS-ROSEA-LIKE DERMATITIS FOLLOWING GOLD THERAPY

REPORT OF TWO CASES

UDO J. WILE, M.D.
Professor of Dermatology and Syphilology
AND
CHARLES J. COURVILLE, M.D.
Instructor in Dermatology and Syphilology
ANN ARBOR, MICH.

Chrysotherapy has been employed with encouraging results in the constitutional treatment of arthritis, lupus erythematosus and various forms of tuberculosis for the past twenty-five or more years. However, the use of gold has been attended in many instances by accidents of varying degrees of severity. Dermatitis has been a frequent manifestation of toxicity. Recent observation of 2 unusual cases in which there were eruptions similar to pityriasis rosea accompanied by lesions on the mucous membranes appearing during gold therapy has stimulated our interest in this subject.

Gold was first used therapeutically in 1810 by Chrestien for the treatment of pulmonary tuberculosis.[1] Koch showed that the presence of gold was lethal to the tubercle bacillus in vitro in 1890. This apparently stimulated others to further investigation for suitable therapeutic forms of gold and their effect on various diseases. Bruck and Glück[2] were the first in recent years to attempt treatment of tuberculosis by gold, using a potassium gold cyanide compound in cases of lupus vulgaris. Speiss and Feldt[3] separately and together reported the use of various gold compounds in tuberculosis between 1912 and 1916. In 1917 Feldt synthesized the compound "krysolgan," which has since been used in Germany and elsewhere for many years in the treatment of

---

Studies and contributions from the Department of Dermatology and Syphilology, University of Michigan Medical School, service of Dr. Udo J. Wile.

1. Cited by Franklin, J. L.: Treatment of Lupus Erythematosus with Sanocrysin, Brit. J. Dermat. **46**:66 (Feb.) 1934.

2. Bruck, C., and Glück, A.: Ueber die Wirkung von intravenösen Infusionen mit Aurium-Kalium cynatum (Merck) bei äusserer Tuberkulose und Lues, München. med. Wchnschr. **60**:57, 1913; abstracted, J. Cutan. Dis. **31**:1058, 1913.

3. Cited by Schamberg and Wright.[6]

cutaneous and other forms of tuberculosis. Ruete,[4] in 1913, used a gold and potassium cyanide compound for the treatment of lupus erythematosus, and Martenstein [5] followed in 1922, reporting on a rather extensive series of patients with lupus erythematosus treated by the gold thiophenol compound (krysolgan) produced by Feldt. Schamberg and Wright [6] introduced into this country gold therapy of lupus erythematosus. Much of the present knowledge concerning the pharmacology and therapeutics of gold is owed to Mollgaard,[7] who reported in 1924 the use of "sanocrysin" (gold and sodium thiosulfate) for the treatment of pulmonary tuberculosis. Feldt [8] used gold experimentally in the treatment of arthritis in 1926. Later it was employed in a large number of cases by Forrestier,[9] Hartfall and Garland,[10] Bach,[11] Pemberton [12] and many others.

Nearly all of the writers cited have reported along with their results of gold therapy various toxic reactions which occurred during the course of treatment. The incidence of toxic reactions has varied with different observers. Copeman and Tegner [13] stated that the importance of accidents has been overemphasized. Mayer [14] found reactions in 10 per cent of 1,400 patients with tuberculosis treated with gold; these

---

4. Ruete, A.: Ueber den Wert des Aurium-Kalium cyanatum bei der Behandlung des Lupus vulgaris und Erythematodes, Deutsche med. Wchnschr. **36**:1727 (Sept. 4) 1913.

5. Martenstein, H.: Die Behandlung des Lupus erythematodes mit Krysolgan, Klin. Wchnschr. **1**:2235 (Nov. 4) 1922.

6. Schamberg, J. F., and Wright, C.: Use of Gold and Sodium Thiosulfate in the Treatment of Lupus Erythematosus, Arch. Dermat. & Syph. **15**:119 (Feb.) 1927.

7. Mollgaard, H.: Chemotherapy of Tuberculosis, Copenhagen, A. Busck, 1924; The Theoretical Basis for the Sanocrysin Treatment of Tuberculosis, Brit. M. J. **1**:643 (April 4) 1925.

8. Cited by Copeman and Tegner.[13]

9. Forrestier, J.: Treatment of Rheumatoid Arthritis with Gold Salt Injection, Lancet **1**:441 (Feb. 27) 1932.

10. Hartfall, S. J., and Garland, H. G.: Gold Treatment of Rheumatoid Arthritis, Lancet **2**:8 (July 6) 1935; Reactions Following Gold Injections, Brit. M. J. **1**: 276 (Feb. 9) 1935; Further Observations on Gold Treatment of Rheumatoid Arthritis, Lancet **1**:1459 (June 27) 1936. Hartfall, S. J.; Garland, H. G., and Goldie, W.: Gold Treatment of Arthritis: Review of Nine Hundred Cases, ibid. **2**:184 (Oct. 2); 838 (Oct. 9) 1937.

11. Bach, F.: Gold in the Treatment of the Rheumatic Diseases, St. Barth. Hosp. J. **43**:206 (Aug.) 1936.

12. Pemberton, H. S.: One Hundred Cases of Chronic Arthritis Treated with Gold, Lancet **1**:1037 (May 4) 1935.

13. Copeman, W. S. C., and Tegner, W.: Review of Gold Therapy, Lancet **1**: 554 (March 6) 1937.

14. Mayer, C.: Gold Treatment of Pulmonary Tuberculosis, Brit. J. Tuberc. **28**:131 (July) 1934.

were mild for the most part. Crosby [15] stated that accidents are of high incidence in spite of care and felt that they have been "glossed over" in reports. Towle,[16] in reviewing the results of gold therapy in 266 cases of lupus erythematosus in America, noted untoward reactions in 14.3 per cent. Hartfall and Garland [10] noted toxic reactions in 41.9 per cent of 900 cases of arthritis, and in 35.3 per cent the reactions were so serious that therapy was stopped.

The accidents occurring during gold therapy have been described by several observers.[17] In general, the reactions have been classified as follows: local, at the site of injection; focal, at the seat of the inflammatory process, and general, or systemic. The last group includes the immediate reactions, such as malaise, pyrexia and gastrointestinal disturbance. Albuminuria has occurred fairly frequently. There have been instances of involvement of the central and peripheral nervous systems. Reactions in the bone marrow, as evidenced by purpura and aplastic anemia, have often been described and frequently have terminated fatally. Dermatitis has been a frequent observation.

The relative incidence of reactions involving the skin and mucous membranes compared to other types of reactions has been high, according to most observers. Hartfall and Garland [10] found that 69 per cent of all patients with toxic manifestations had cutaneous reactions alone or in association with others. The majority of cutaneous reactions developed during treatment, but in 21 per cent they appeared from one to twelve weeks after treatment had been discontinued. The cutaneous reactions in general resemble those associated with other heavy metals, such as arsenic, bismuth and mercury. Pruritus, generalized or localized, has been noted by many observers. This may be severe and associated with erythema which may be persistent or transient. Urticaria may occur. The erythema may progress to exfoliative dermatitis which has terminated fatally in some instances, but recovery is the rule. Morbilliform and scarlatiniform eruptions are relatively common, as well as papular and papulosquamous lesions. The dermatitis sometimes becomes eczematous. Vesicular and bullous lesions have been described in some cases as appearing similar to herpes simplex or zoster. Hyperkeratoses have been observed as late sequelae.

Lesions of the mucous membranes have been described on many occasions. Metallic taste in the mouth is noted occasionally as a warning

---

15. Crosby, G. J. V.: Accidents of Gold Treatment of Rheumatoid Arthritis, Lancet **1**:1463 (June 27) 1936.

16. Towle, H. P.: The Present Status of Gold Therapy, New England J. Med. **204**:487 (March 5) 1937.

17. Driver, J. R., and Weller, J. N.: Untoward Results from the Use of Gold Compounds, Arch. Dermat. & Syph. **23**:87 (Jan.) 1931. Pemberton.[12]

of more serious damage. Loss of sensation of taste for a period of time has been reported.[18] Congestion of the fauces and redness of the buccal mucosa have been observed, and these have progressed to erosive and ulcerative stomatitis which has been severe enough to interfere seriously with nutrition. In addition, ulcerative gingivitis and pharyngitis have caused dysphagia in some cases. Involvement of the conjunctiva and cornea have been mentioned by some observers alone and in association with other findings. Ketron [19] described a patient treated by gold and sodium thiosulfate for lupus erythematosus in whom bullous erythema multiforme developed with stomatitis, conjunctivitis and keratitis which went on to corneal scarring and permanent blindness.

Cutaneous lesions of rather unusual types have been reported. Moore [18] observed shining particles of gold on the volar surfaces of the finger tips of a patient seven minutes after an intramuscular injection of aurothiodextrose on two occasions. Throne, Kingsbury and Meyers [20] reported 2 cases in which lesions developed that were identical with lichen spinulosus during gold therapy. Pillsbury and Kulchar [21] presented 2 patients with vitiligo in whom after they received gold and sodium thiosulfate a prolonged dry scaling erythematous eruption developed only on depigmented areas of the body. Roche [22] mentioned a patient in whom giant urticaria developed. Schamberg [23] cited a case in which a solution of colloidal gold had accidentally been injected outside the vein, with a resultant greenish blue discoloration which persisted for at least six months. Boon [24] reported a case of alopecia, stomatitis and exfoliation of the nails. Mayer [14] stated that in 2 per cent of 1,400 patients treated with gold and sodium thiosulfate for tuberculosis lilac blue pigmentation developed limited to the exposed areas or areas exposed to ultraviolet rays. This pigmentation persisted for a long time

18. Moore, T.: Reactions Following Gold Injections, Brit. M. J. **1**:389 (Feb. 3) 1935.

19. Ketron, in discussion on Munson: Lupus Erythematosus, Arch. Dermat. & Syph. **17**:742 (May) 1928.

20. Throne, B.; Kingsbury, J., and Meyers, C. N.: Unusual Clinical Manifestations Following Intravenous Administrations of Gold Compounds, Arch. Dermat. & Syph. **25**:494 (March) 1932.

21. Pillsbury, D. M., and Kulchar, G. V.: Gold Dermatitis Limited to Depigmented Skin, Arch. Dermat. & Syph. **27**:36 (Jan.) 1933.

22. Roche, H.: Precautions in Sanocrysin Therapy, Brit. M. J. **1**:31 (Jan. 4) 1936.

23. Schamberg, J. F.: Chrysoderma, Arch. Dermat. & Syph. **18**:862 (Dec.) 1928.

24. Boon, T. H.: Complications of Gold Therapy, Brit. M. J. **1**:780 (April 9) 1938.

but ultimately disappeared. Reactions of the skin similar to lichen planus have been reported by Pautrier and Roederer [25] and by Milian.[26]

We were able to find only 3 cases in which lesions similar to pityriasis rosea followed gold therapy. Simons [27] merely mentioned that in a patient with lupus erythematosus treated with gold an eruption developed which was similar to pityriasis rosea. Kiess [28] reported a pityriasis-rosea-like eruption occurring in a 33 year old woman after she received 1.6 Gm. of aurophos for lupus vulgaris. Rattner [29] stated that he saw an eruption resembling pityriasis rosea in a patient following gold treatment for lupus erythematosus.

During the past eight months we have encountered 6 cases of dermatitis of various types which we have attributed to gold therapy. In 2 of these cases the eruptions have been similar to pityriasis rosea, and because this manifestation is so unusual we have felt it worth while to draw attention to them.

REPORT OF CASES

CASE. 1.—L. C., a 46 year old English housewife, had been treated at the Rackham arthritis unit of the University of Michigan Medical School for the past year for atrophic arthritis of eight years' duration. Her past history revealed fair general health and occasional attacks of urticaria.

On Aug. 24, 1939 intramuscular gold therapy was started with myochrysin (gold sodium thiomalate), which was given weekly, the dose beginning with 10 mg. and increasing each week until 100 mg. was given in the fifth injection. This dosage was maintained for thirteen weeks, at which time she had received a total of 1,010 mg. of the drug. A few minutes after having received the twelfth injection redness of the conjunctiva, flushing of the face, perspiration of the brow, faintness and apprehension developed. This was followed by a burning sensation in the eyes, which persisted for three days. Two weeks after the final injection she began to complain of sore mouth. Two weeks later she noted a pruritic scaling eruption of the scalp, and the following week a fairly generalized rash involving mainly the shoulders and trunk appeared.

Shortly after this, she was seen in the dermatologic clinic, where examination revealed a widespread, only slightly inflammatory, dry, scaling, patchy eruption of the scalp. Confined to the trunk was a mildly erythematous eruption, composed of papulosquamous lesions with fine scales, which was most evident in the midline

---

25. Pautrier, L. M., and Roederer, J.: Aurides lichéniennes verruqueuses en nodules isolés et en placards, végétants, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Strasbourg) **45**:139 (Feb.) 1938.

26. Milian, G.: Le lichen plan aurique, Bull. Soc. franç. de dermat. et syph. [**46**]:38 (Jan.) 1939. Schneidewind, A.; Albertal, M., and Trajtenberg, S.: Crisiasis, Rev. Asoc. méd. argent. **52**:792 (Aug. 15) 1938.

27. Simons, R.: Twenty-Five Years of Gold Treatment of Lupus Erythematosus, Brit. J. Dermat. **50**:575 (Nov.) 1938.

28. Kiess, O.: Ueber eine der Pityriasis rosea "ähnliche unter Pigmentierung abheilende Gold-(Aurophos-) Dermatitis, Dermat. Wchnschr. **86**:133 (Jan. 28) 1928.

29. Rattner, H.: Personal communication to the authors.

posteriorly and tended to sweep around in the lines of cleavage. This eruption was similar to pityriasis rosea. No primary plaque was present. There was a mild hyperkeratosis of the right palm and an erythematous plaque on the left palm. The lower extremities were spared. The breath had a metallic odor, and there were several superficial erosions on the buccal mucous membrane and on the lower lip.

Three weeks later on reexamination considerable loss of hair from the scalp was noted. There were postauricular erythema and scaling. The mouth remained about the same. The eruption on the trunk had spread to involve the upper portions of the extremities.

On March 17, 1940 she was presented at the joint meeting of the Chicago and Detroit dermatologic societies in Ann Arbor.[30] Examination at this time revealed a greasy scaling eruption of the scalp with postauricular extension, erythema about the eyes and periumbilical erythema and scaling. The same scaling maculopapular lesions were noted on the back, but in the axillas there were elongated scaly,

Results of Studies of the Blood

	Blood Cells per Cu. Mm.			Differential Count, in per Cent				
Date	Red	White	Hemoglobin, per Cent	Polymorphonuclear Leukocytes	Basophils	Eosinophils	Lymphocytes	Mononuclear Leukocytes
8/ 1/39*	3,400,000	5,000	76	70	0	3	25	2
10/11/39	4,450,000	3,600	77	80	0	4	13	3
11/18/39 †	.....	3,500	74	..	..	..	..	..
11/25/39	.....	4,800	75	..	..	..	..	..
1/ 4/40 ‡	.....	4,450	80	77	0	2	18	3
5/31/40	.....	4,500	78	..	..	..	..	..

* Before gold was administered.
† At the time of first symptom of intolerance of gold.
‡ At the time of first examination following onset of reaction.

crinkled, stria-like lesions. There was a patch of lichenoid papules on the anterior surface of the left wrist. The lesions of the mucous membranes were about the same as previously noted.

On May 31 she was again examined. At this time no lesions of the mouth were noted. The eruption on the body had subsided, leaving residual pigmentation and slight atrophy at the sites of previous lesions.

Laboratory Data.—The Kahn reaction of the blood was negative. The urine was normal throughout the period of observation.

CASE 2.—O. L., a 54 year old white farmer, was being treated at the Rackham arthritis unit of the University of Michigan Medical School for chronic active atrophic arthritis. On August 18, 1939 intramuscular gold therapy with myochrysin was instituted. He received injections beginning with 10 mg., gradually increasing to 100 mg. and continuing with this dosage. On October 16, after having received 630 mg., he complained of moderate pruritus of the legs; this was not made worse by further treatment. On November 25, at which time he had received a total of 1,230 mg., he complained of a severe generalized pruritic dermatitis, swelling of the eyelids and sore mouth. Injections were discontinued at this time.

30. Wile, U. J.: Gold Dermatitis and Stomatitis, Arch. Dermat. & Syph. **42**: 721 (Oct.) 1940.

Two weeks later he was examined in the dermatologic clinic and presented a slightly erythematous papulosquamous eruption on the trunk and proximal portions of the extremities. The characteristic lesions were round or oval, slightly elevated, discrete and covered by a branny type of scale. On the chest and back the lesions followed the lines of cleavage. There was no evidence of a herald plaque. Many of the lesions had been excoriated and were covered by hemorrhagic crusts. The face was erythematous. There was a gray membrane on the upper lip. The lower

Ulcerative lesions of the lips (case 2).

Blood Studies

Date	Blood Cells per Cu. Mm.		Hemoglobin, per Cent	Differential Count, in per Cent				
	Red	White		Polymorphonuclear Leukocytes	Basophils	Eosinophils	Lymphocytes	Mononuclear Leukocytes
8/15/39 *	4,100,000	9,800	79	69	0	1	26	4
10/16/39 †	3,700,000	6,400	82	..	..	..	..	..
10/24/39	.....	8,400	84	..	..	..	..	..
12/11/39 ‡	4,930,000	8,500	85	75	0	1	16	8

* Before gold was administered.
† At time of first complaint of pruritus.
‡ Seventeen days after onset of severe pruritus.

lip was covered by a yellowish brown crust, and there were many fissures, especially at the angles of the mouth. The eyelids were erythematous and edematous and were covered by a branny type of scale. There were crusting of the margins of the lids and mild hyperemia of the conjunctivas.

With bland topical treatment and intravenous injections of sodium thiosulfate the symptoms sufficiently improved to warrant the patient's discharge from the hospital in ten days. He stated in a letter one month later that his eruption had entirely disappeared.

Laboratory Data.—The Kahn reaction of the blood was negative. The urine was normal throughout the period of observation except for a few white blood cells.

COMMENT

The question might be raised as to whether or not the condition in these cases was latent or incubating pityriasis rosea made manifest clinically by the stimulation of injections of a gold compound. The following facts point against this concept: There was no initial lesion or plaque; the lesions of the mucous membranes were a definite part of the picture and are rarely, if ever, seen in pityriasis rosea, and there were pruritus and scaling of the scalp, with diffuse alopecia and palmar lesions in 1 case.

We felt that these patients presented cutaneous reactions due to intolerance to gold used therapeutically. If this is true, the accidents may be due either to overdosage or to individual hypersensitivity to the drug. Furthermore, we are unable to suggest any certain means of prevention or foretelling the occurrence of toxic reactions. The fact that the reaction occurred two weeks after the last injection in 1 case suggests that there is a cumulative action and warns against the use of large doses. Frequent urinalysis was no help in predicting these accidents. It is, however, important because of the possibility of renal involvement. The white blood count was significantly lowered in 1 of the cases, and undoubtedly the blood picture should be followed in all patients receiving gold to avoid depression of the bone marrow. The sedimentation rate is probably of little value as a prognostic aid in gold intolerance, since it is lowered if the course of the infectious process is favorable. Several writers, including Wilson,[31] have advised the use of calcium with gold to prevent the occurrence of untoward sequelae. This has not been tried here. The administration of large doses of vitamins A, B and C as a prophylactic measure was suggested by Secher.[32] Undoubtedly gold should not be used when the disease process is acute.

SUMMARY

Reports on 2 patients are presented, in whom lesions of the mucous membranes and a dermatitis similar to pityriasis rosea developed while they were receiving intramuscular injections of myochrysin for arthritis.

Most of the recent literature on cutaneous reactions to gold is briefly reviewed.

Dr. Richard Freyberg, of the Rackhan Arithritis Unit, cooperated in this study.

31. Wilson, J.: Prophylaxis of Severe Reactions in Gold Salt Therapy, Tubercle **18**:168 (Jan.) 1937.

32. Secher, K.: Prevention of Complications During Gold Therapy of Tuberculosis and Arthritis, Lancet **1**:996 (April 30) 1938.

HEREDITARY EDEMA OF THE LEGS (MILROY'S DISEASE)

ASSOCIATED WITH OTHER CONGENITAL ANOMALIES

WILLIAM A. ROSENBERG, M.D.
CHICAGO

A case of hereditary edema of the legs with other congenital anomalies recently came under my observation. Hereditary edema of the legs being rare, its combination with other congenital anomalies warrants reporting this case as one of unusual interest.

REPORT OF A CASE

L. L., a white woman aged 28, was first seen at the Northwestern University Medical School on April 15, 1939. She stated that her limbs had been enlarged since infancy and that her mother and an aunt had the same condition. The enlargement appeared soon after her birth and gradually progressed during her growth and development. She had experienced no discomfort until about one and one-half years before her appearance at the clinic, when painful swelling of both feet developed, more evident during the afternoon and evening. Rest at night, however, did not materially reduce the swelling or relieve the pain. Properly fitted shoes were prescribed and worn, and as a result the painful edema practically disappeared. The original enlargement of the limbs, however, persisted.

Examination revealed a well nourished, intelligent woman, 5 feet and 3 inches (160 cm.) in height, weighing 184 pounds (83.5 Kg.) and having slightly dry but otherwise normal skin. The hair of the scalp was fine, scant and blond so that the scalp could easily be seen through the sparse growth, particularly over the vertex, a condition which had been present since childhood. The head was normal in contour. The left eye was blind and had been since infancy; it showed a slight strabismus, for which an operation had been performed when she was 11 or 12 years old. She stated that her teeth had come in crooked and far apart. The upper teeth had been extracted because of poor condition. The lower incisor and canine deciduous teeth had fallen out and had never been replaced. The two upper first deciduous incisors had remained as baby teeth until extracted.

The heart and lungs were normal. Her blood pressure was 120 systolic and 60 diastolic. The abdominal, gastrointestinal and genitourinary examinations gave essentially negative results. The hands were puffy and cold. The lower extremities were thickened from the knees down, the circumference being 12 inches (30.5

From the Department of Dermatology and Syphilology, Northwestern University Medical School, Arthur W. Stillians, M.D., Director.

cm.) at the ankle and 17 inches (43 cm.) at the calf. The skin over the thickened limbs was normal, with no pitting on pressure. The left foot had six toes.

The urine was normal. A blood count showed 80 per cent hemoglobin and 3,890,000 erythrocytes and 10,690 leukocytes per cubic millimeter, with a normal differential count. The basal metabolic rate was —13 per cent. The Wassermann reaction of the blood was negative. Chemical analysis of the blood showed 116.9 mg. of sugar, 10.8 mg. of calcium, 3.53 mg. of phosphorus and 494 mg. of chlorides per hundred cubic centimeters. The carbon dioxide-combining power was 37.9 cc. per hundred cubic centimeters.

Fig. 1.—Symmetric thickening from the knees down.

Roentgenograms of the feet revealed no abnormality of the right foot but showed two proximal phalanges articulated with the second metatarsal bone on the left foot. The sella turcica was round and within normal limits as to size. It measured 12 mm. in its longest diameter. There was no evidence of a skeletal anomaly of either hand.

CLINICAL FEATURES

Special Features.—The unusual features in this case not previously reported were: retention of the deciduous teeth, six toes on the left foot, congenital strabismus with amblyopia of the left eye and distrophy of the hair. Other concurrent features, such as hydrocele, have been reported

by Boks [1] and by van Vliet.[2] Faber and Lusignan [3] reported a case of hereditary elephantiasis with a hydrocele and spina bifida occulta.

Description.—The disease consists of enlargement of the soft tissues of one or more extremities, usually the lower, associated with firm edema of the affected parts. The enlargement is due mainly to compression and hypertrophy of the connective tissue and to the presence of numerous dilated channels in the cutis. Roentgen examinations show no thickening of the bones. A hereditary element is present in the majority of cases. In the family reported by Milroy [4] the disease occurred in six

Fig. 2.—Sparse growth of hair.

successive generations. The cases fall into two groups: those in which swelling is present at birth and those in which it may occur in childhood, at puberty or even during early adult life.

1. Boks, D. B.: Congenital Familial Edema of the Lower Extremities, Nederl. tijdschr. v. geneesk. **1**:416, 1913.

2. van Vliet, J. C.: Congenital Edema of the Lower Extremities in One Family, Nederl. tijdschr. v. geneesk. **2**:1092, 1913.

3. Faber, H. K., and Lusignan, H. R.: Hereditary Elephantiasis, Am. J. Dis. Child. **46**:816 (Oct.) 1933.

4. Milroy, F. W.: Chronic Hereditary Edema, J. A. M. A. **91**:1172 (Oct. 20) 1928.

Acute Attacks.—An unusual feature of the disease consists of acute attacks of chills and fever, with hyperemia, edema, swelling and pain of the affected extremities. The condition during these attacks sometimes resembles erysipelas and occasionally is described as lymphangitis. The attacks were first noted by Meige.[5] Later they were noted by Hope and French [6] in many of their series, by Hamman [7] and by Brandt [8] in 5 of his 13 cases. Acute attacks have been chiefly confined to cases in which the characteristic swelling of the extremities has appeared some time after birth.

HISTORICAL REVIEW

Milroy [9] in 1892 described in detail 22 cases occurring in six generations of a family consisting of 97 persons. The condition is frequently called Milroy's disease in this country. Meige [5] in 1898 reported 8 cases in four generations of a family. The disease is frequently referred to as Meige's disease in France. Similar cases were reported by Hille [10] in 1841. Nonne [11] in 1890 reported 4 cases of elephantiasis congenita hereditaria in one family and stated that he could find no previous report of similar cases. Desnos [12] in 1891 also indicated the possibility of heredity as a cause of edema when he reported a case and remarked that the condition was more frequent in females and, from a hereditary point of view, more often found in the maternal line. Griffith and Newcomet [13] reported a case of a condition that they regarded as allied in some respect to Milroy's disease; a child, aged 4 years, had edema of the face and of the left leg which developed at 3 months of age. Weber and Schlüter [14] recorded late onset in 2 sisters, the condition beginning when they were 20 and 22. Hope and French [6] also described

5. Meige, H.: Dystrophie oedémateuse héréditaire, Presse méd. **2**:341, 1898.

6. Hope, W. B., and French, H.: Persistent Hereditary Oedema of the Legs, Quart. J. Med. **1**:312, 1908.

7. Hamman, L.: Milroy's Disease, M. Clin. North America **1**:182, 1917.

8. Brandt, G.: Ueber familiäre Elephantiasis cruris, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **37**:56, 1923.

9. Milroy, F. W.: An Undescribed Variety of Hereditary Edema, New York M. J. **56**:505, 1892.

10. Hille, J.: Ueber die Elephantiasis, Wchnschr. f. d. ges. Heilk., 1841, pp. 433 and 457; cited by Brandt.[8]

11. Nonne, M.: Vier Fälle von Elephantiasis congenita hereditaria, Virchows Arch. f. path. Anat. **125**:189, 1890.

12. Desnos: Oedeme rhumatismal chronique, Bull. et mém. Soc. méd. d. hôp. de Paris **3**:65-73, 1891.

13. Griffith, J. P. C., and Newcomet, W. S.: Types of Oedema in Infancy and Childhood, Tr. A. Am. Physicians **12**:399, 1897.

14. Weber, F. P., and Schlüter, A.: Nonne-Milroy-Meige Oedema, of Late Onset, in Sisters, Proc. Roy. Soc. Med. **30**:933, 1937.

a case of the disease in a child aged 3 months, and Lannois [15] reported a case in which the patient was 14 months of age. Debove [16] in 1902 reported a case of segmentary edema in a woman aged 25 who had suffered from swelling of the lower part of the left leg since the age of 8 years. The swelling was not uniform but was limited to segments of the foot, leg and thigh.

PATHOLOGY AND PATHOGENESIS

Among the hypotheses that have been advanced is the theory of Meige,[17] who stated the belief that there is a congenital malformation of the trophic centers in the spinal cord regulating the growth of cellular tissue. Rapin [18] postulated an embryonic dyscrasia of the mesoblast. Valobra [19] implicated the nervous center controlling the secretion of lymph. Spiller [20] speculated on the role played by the vasomotor nerves in the causation of the edema, while some authors attributed the condition to endocrinopathy.

Microscopic examination of the affected part of the leg has been made only a few times. Stoesser [21] stated that there is a fibrosis in the subcutaneous tissue. Sussini and Casaubón [22] gave a more detailed description. They noted that the epidermis is apparently redundant. The cutis consists of dense fasciculated connective tissue containing islands and foci of cells, the latter often perivascular. The panniculus is segmented by dense layers of fibrous tissue. Elterich and Yount [23] in their case noted extensive fibrosis replacing the subcutaneous tissue.

15. Lannois, M.: Une observation de trophœdème chronique héréditaire, Nouv. iconog. de la Salpêtrière **13**:631, 1900; Hereditary Chronic Oedema of the Lower Limbs, M. Rev. **4**:99, 1901.

16. Debove: Oedème segmentaire des membres inférieurs, Bull. et mém. Soc. méd. d. hôp. de Paris **14**:1172, 1897.

17. Meige, H.: Le trophoedème chronique héréditaire, Nouv. iconog. de la Salpêtrière **12**:453, 1899.

18. Rapin, E.: Sur une forme d'hypertrophie des membres, Nouv. iconog. de la Salpêtrière **14**:472, 1901.

19. Valobra, I.: Les oedèmes circonscrits aigus et chroniques sous la dépendance du système nerveux (rôle de la sécrétion lymphatique dans leur pathogénie), Nouv. iconog. de la Salpêtrière **18**:201 and 255, 1905.

20. Spiller, cited by Ayala, G.: Le trophoedème chronique et le système endocrinosympathique, Encéphale **1**:319, 1913.

21. Stoesser, A. V.: The Hypertrophies of Infancy and Childhood, Am. J. Dis. Child. **35**:885 (May) 1928.

22. Sussini, M., and Casaubón, A.: Trofoedema crónico de Meige: Resultados quirúrgicos, Rev. de especialid. **1**:474, 1926.

23. Elterich, T., and Yount, C. C.: Congenital Elephantiasis, Am. J. Dis. Child. **29**:59 (Jan.) 1925.

Fig. 3.—Lower incisors and canine deciduous teeth had fallen out and had never been replaced.

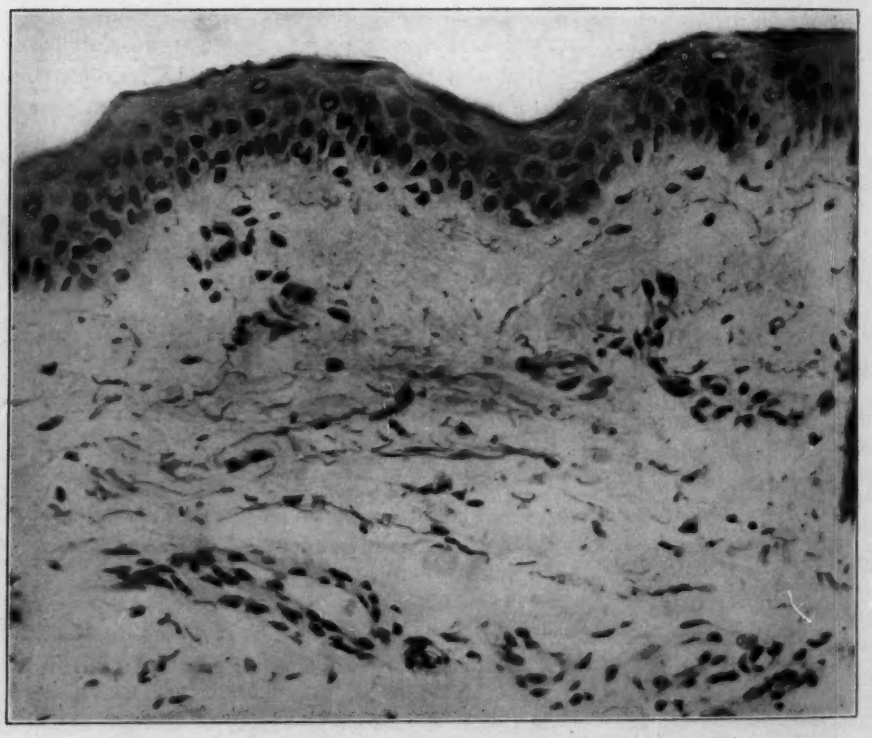


Fig. 4.—Photomicrograph showing elastic tissue fibers (× 325).

Throughout these sections there was a mononuclear perivascular exudate in the affected fatty tissue. McGuire and Zeek [24] studied sections of the skin from 2 patients. The epidermis in 1 case was normal and in the other slightly thickened; the corium, and especially the hypoderm, showed severe edema in which pools of fluid were present in spaces

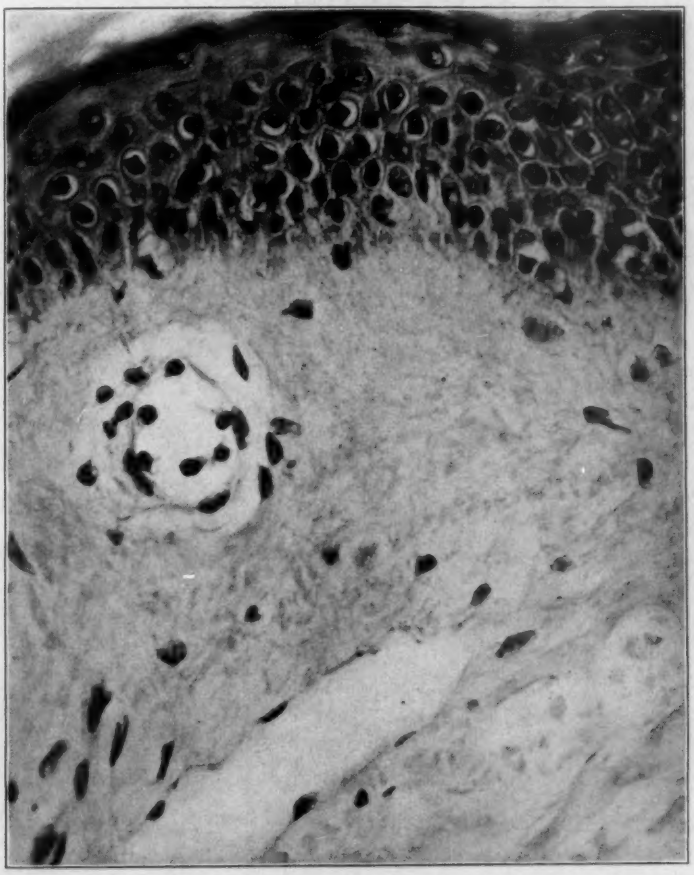


Fig. 5.—Photomicrograph showing vesicular dilatation (× 1,000).

devoid of endothelial lining. They observed decided condensation of the papillary corium with some hyaline degeneration of the collagen, absence of the elastica and slight perivascular lymphocytic cellular infiltration.

24. McGuire, J., and Zeek, P.: Pathogenesis of Chronic Hereditary Edema of Extremities (Milroy's Disease), J. A. M. A. **98**:870 (March 12) 1932.

A biopsy specimen was taken from the calf of the right leg in the case reported, and the histologic sections were studied by T. K. Lawless, who gave the following detailed report:

The stratum corneum is moderately hypertrophic, with no evidence of abnormal keratinization taking place. The granular layer is one cell in width through the entire section. The mucous layer is abnormally rich in cells characterized by vacuolar degeneration. The basal layer shows not only vacuolar degeneration but cellular separation due to increased edema. The basal line is almost straight. The principal changes in this condition take place in the corium. The papillary

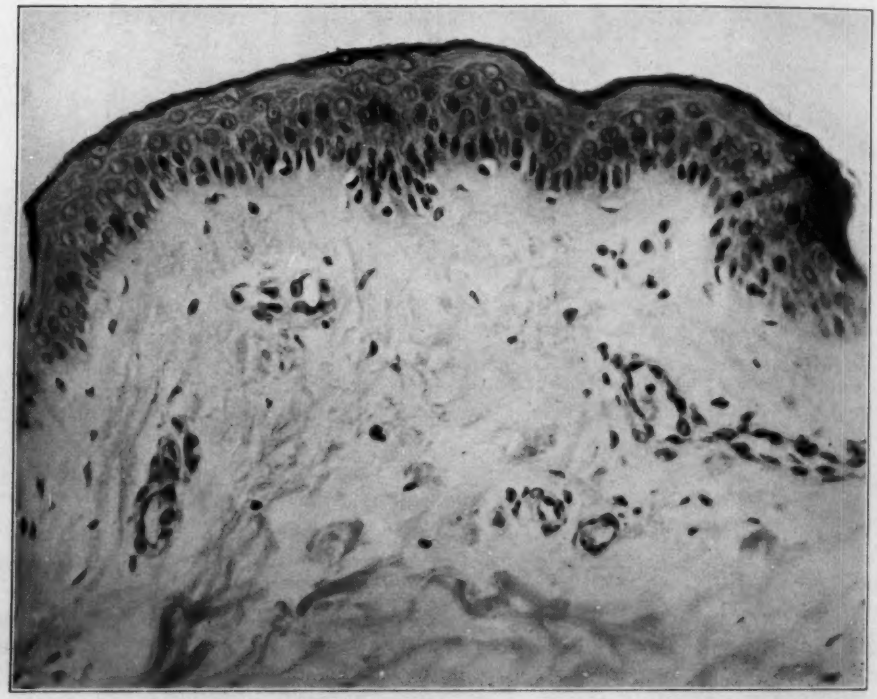


Fig. 6.—Photomicrograph showing fibrosis and lymphatic dilatation (× 300).

and subpapillary parts show a compression of the fibers with definite hypertrophy. The edema is pronounced, with many large, dilated channels without definite cellular walls. The elastic tissue, though showing signs of degeneration, is much in evidence. Blood vessels are present. They have thicker walls without perivascular infiltration. The reticular layer shows both hypertrophy and hyperplasia. The heavy collagenous fibers appear as short segments and show moderate degeneration. Edema is pronounced. The vessels are thickened, and the cellular reaction is slight. The subcutaneous tissue is characterized by the enormous open spaces, the paucity of normal cells and fatty infiltration. The appendages are all normal in appearance. The elastic tissue is fragmented and takes the stain poorly.

TREATMENT

A patient with an acute attack should be treated like one with an acute infection with local manifestations. When the deformity is great, the modified Kondoleon [25] operation is recommended. Properly fitted shoes gave my patient considerable relief. Rest and elevation of the legs at frequent intervals seem to be all that is needed in most cases.

SUMMARY AND CONCLUSIONS

Hereditary elephantiasis of the legs, generally known in this country as Milroy's disease, shows microscopically hypertrophy and increase of the connective tissue in the cutis, with edema and many dilated channels without cellular walls.

Two groups of cases can be recognized: (1) those in which the swelling is present at birth and (2) those in which the swelling appears in late childhood or in early adult life. The acute attacks are practically confined to the second group.

The case herein described belongs to the congenital group, and there were associated congenital anomalies which had not been previously noted, such as retention of the deciduous teeth, six toes on the left foot, congenital strabismus with amblyopia of the left eye and dystrophy of the hair.

---

25. Homans, J.: The Treatment of Elephantiasis of the Legs, New England J. Med. **215**:1099, 1936.

Clinical Notes

ULCERATIVE REACTION FROM GENTIAN VIOLET IN THE TREATMENT OF IMPETIGO CONTAGIOSA

LEON GOLDMAN, M.D., CINCINNATI

Permanent scarring following uncomplicated impetigo contagiosa is rare. With the use of the occlusive method of treatment of impetigo with such agents as adhesive plaster or the less effective collodion, no deep extension of the lesion to an ecthymatiform ulcer has been observed. With the crusting type of therapy, no such ulcerations have been seen with silver nitrate, cupric sulfate or tannic acid–mercury preparations.

However, with the gentian violet crusting method this reaction has occurred occasionally in the past two years. It has been seen in 4 cases, in 2 infants and 2 adults. In these cases a smooth gentian violet crust formed over the impetigo areas. Instead of curling up, shrinking and peeling off, as the usual gentian violet crust does, the crusts in these instances remained fixed firmly to the skin for a relatively long period, more than two weeks and in 1 case five weeks. The skin adjacent to the adherent crust showed no redness, tenderness or edema. However, when the crust was removed, either with wet dressings or with scissors and forceps, a deeply punched-out area filled with pus was found. With irrigation and application of mercury ointments these areas healed rather rapidly but left ugly punched-out scars, some resembling a postvaricella scar and others the depressed scar of an ecthymatous ulcer. These were seen chiefly on the face and, in 1 infant, deep in the axilla. There was no evidence of hypersensitivity to gentian violet in any of the cases.

In 3 of the cases the solution of gentian violet used was a saturated alcoholic solution, containing approximately 30 per cent gentian violet. In 1 case, that of an adult, there were small depressed scars following impetigo spots treated with a 1 per cent aqueous solution of gentian violet. Other lesions on this patient's face, treated with 5 per cent ammoniated mercury ointment, showed no scars. The saturated alcoholic solution of gentian violet was used because of its excellent results in cases of impetigo of Bockhart and of pustular miliaria. Originally, it seemed to be desirable in impetigo contagiosa, in spite of the transient pain, because a firm heavy dry crust forms over the entire lesion in a few seconds to a few minutes, whereas the impetigo lesion treated with repeated applications of an aqueous solution of gentian violet continues to ooze for several hours. No bacteriologic studies were made of the material under the gentian violet crust.

In the gentian violet therapy of burns, when this form of therapy was more popular than it is today I would frequently observe failure of healing under the firm gentian violet crust but only rarely see persistent infection with deeper extension. I have had no experience with the gentian violet–silver nitrate treatment of burns.

This complication of the gentian violet treatment of impetigo contagiosa must be uncommon when one considers the popularity of this method. From the small group of cases here, the saturated alcoholic solution of gentian violet is much more apt to cause this. The complication should be suspected when there is no evidence of separation of a gentian violet crust after an arbitrary period of approximately

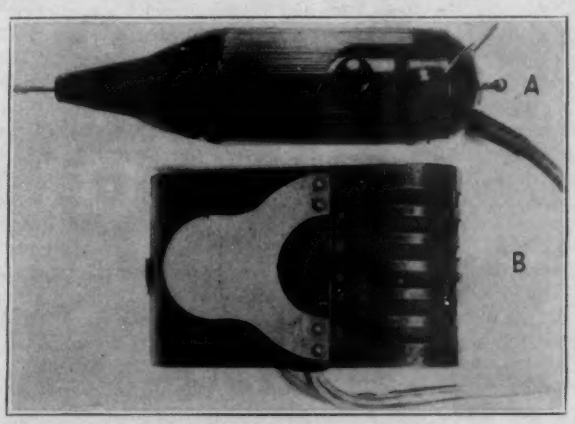
two weeks. This clinical survey does not suggest any reason why this reaction has occurred with gentian violet and not with the other occlusive or crusting methods. Perhaps if the other methods had been used as frequently as the gentian violet treatment, this unusual complication would have been encountered.

Carew Tower.

THE USE OF A DRILL ON DISEASED NAILS

ROY L. KILE, M.D., AND ASHTON L. WELSH, M.D., CINCINNATI

For many years chiropodists have used a drill for removing diseased nails and at times horny tissue from the feet. For some time we also have employed a drill for grinding away diseased nails. To the best of our knowledge, such an



A, a drill for grinding away diseased nails. *B*, a foot-controlled rheostat for regulating the speed of the drill.

instrument is not in general use by dermatologists. It is not expensive and may be equipped with a foot-controlled rheostat for regulating the speed. Steel or emery burrs of various shapes and sizes may be obtained to fit it. Two or three burrs will suffice for dermatologic purposes.

Diseased nails may be ground away much faster than they can be cut away and without causing any pain. Continuous running will cause the burrs to become warm and consequently cause some pain, but occasional short stops will prevent this. Much better application of drugs or physical therapy to the area is accomplished after the diseased nails are ground away with this or a similar instrument.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

MASSIVE DOSE ARSENOTHERAPY OF SYPHILIS BY THE INTRAVENOUS DRIP METHOD. H. T. HYMAN, L. CHARGIN and W. LEIFER, Am. J. Syph., Gonor. & Ven. Dis. **23**:685 (Nov.) 1939.

Fifteen of the original series of 25 patients with early syphilis who were given massive dose arsenotherapy by the intravenous drip method are still under observation more than five years after treatment. The observations indicate that the massive therapy for five days without any other antisyphilitic treatment resulted in a complete cure in 13 of the 15 patients, or 86.6 per cent.

In the past two years a second series of 86 male patients with primary or secondary syphilis was treated. Four to 4.5 Gm. of neoarsphenamine was administered during four or five days with the identical technic employed in the first series. Dark field examinations of material from moist early lesions showed negative results within twenty-four or forty-eight hours, and the lesions healed promptly. Seventy-eight of the second series are still under observation. Of the 78 patients, 67 (or 86 per cent) are entirely seronegative and are clinically well nine and fifteen months after treatment. The spinal fluids of 60 patients have been examined and are all normal. In 4 cases the treatment may be classified as a failure, and in 7 it gave doubtful results. In 6 of these 7 the result is doubtful because the Wassermann reactions have not as yet become entirely negative. In another man a new penile lesion of doubtful significance developed after he had exposed himself repeatedly to reinfection. Two patients have had a serologic relapse, and 2 others have had a clinical relapse (chancre redux).

Nitritoid crises did not occur in any of the treated patients. Febrile reactions occurred in the majority of the patients and were sometimes severe. A primary fever was present in more than 60 per cent; a secondary fever, usually associated with a toxicoderma, was observed in more than half the patients. Polyneuritis of moderate severity occurred in 10 per cent and was slight in another 25 per cent. There were no disturbances in renal function. One patient suddenly had a convulsion and died.

QUARTAN MALARIA IN THE TREATMENT OF NEUROSYPHILIS. M. M. KROLL, Am. J. Syph., Gonor. & Ven. Dis. **24**:148 (March) 1940.

The author reviews the literature and reports favorably on the use of quartan malaria in the therapy of neurosyphilis. In 5 out of 6 cases of primary atrophy of the optic nerve conservation of existing sight was achieved. No direct correlation was found between clinical and serologic improvement. There was 1 death as a result of quartan malaria in the 62 patients treated.

GRANULOMA INGUINALE. L. J. ALEXANDER and A. G. SCHOCH, Am. J. Syph., Gonor. & Ven. Dis. **24**:180 (March) 1940.

A report of a case of granuloma inguinale is presented in which the pathognomonic giant cells of granuloma inguinale have been demonstrated in sections of tissue. The authors stated the opinion that the Giemsa stain is essential to demonstrate the typical giant cells in biopsy specimens; they were unable to demonstrate these cells with routine hematoxylin and eosin stains.

CHANGES IN THE LONG BONES OF NEWBORN INFANTS FOLLOWING THE ADMINISTRATION OF BISMUTH DURING PREGNANCY. J. WHITRIDGE JR., Am. J. Syph., Gonor. & Ven. Dis. **24**:223 (March) 1940.

The author confirms the previous work of Caffey, who described roentgenologic changes in the long bones of newborn infants whose mothers had received intra-

muscular injections of a bismuth compound during pregnancy as part of their antisyphilitic treatment. The roentgenologic changes consisted of transverse bands of increased density near the ends. The intramuscular administration of a bismuth compound to normal nonsyphilitic pregnant women produced similar changes in the long bones of the newborn infants, independent of the amount of the drug given. The changes are not due to healed syphilitic osteochondritis.

ON THE EFFECT PRODUCED ON NEWLY CONTRACTED SYPHILIS BY THE TRANSFUSION OF BLOOD TAKEN FROM PATIENTS AFFECTED WITH LATE STAGES OF SYPHILIS. M. S. BRAGIN, Am. J. Syph., Gonor. & Ven. Dis. **24**:228 (March) 1940.

Repeated transfusions of blood from patients affected with late untreated syphilis to patients suffering from newly contracted syphilis produced a rather rapid reversal in the Wassermann reaction of the recipients' blood, which was, however, of only a temporary nature. There was no change in the Wassermann reaction of the patients' tissue fluid and but slight effect on the clinical symptoms.

Transfusion of normal blood did not produce any effect on the Wassermann reaction in patients with early syphilis. REUTER, Milwaukee.

SYMPOSIUM ON ALLERGIC DERMATOSES: CONTACT-TYPE ECZEMATOUS DERMATITIS. MARION B. SULZBERGER, J. Allergy **11**:40 (Nov.) 1939.

In the author's opinion, the contact type of eczematous dermatitis is possibly the most common of all diseases of man, and in most instances, it can be proved to be allergic. Not all eczematous dermatoses are of allergic origin. The typical dermatosis produced by certain degrees of sunshine (eczema solare), the eczematous cutaneous lesions which are due to primary irritants, such as caustics, acids and alkalies, and the eczematous reactions from physical agents, such as heat, friction and maceration, are not allergic.

Allergens are usually not proteins or substances necessarily associated with proteins. Even simple chemicals, such as mercury, nickel and arsenic, are capable of sensitizing certain persons. Substances which can most easily penetrate through the natural protective layers of the skin, such as fat solvents, substances soluble in fats, keratolytics or detergents, are the commonest eczematogenous allergens.

The diagnosis of this form of dermatosis depends on the history, the clinical appearance and the course of the eruption, and *only in the last analysis on the results of the cutaneous test.* The results of patch tests are not conclusive; as in other cutaneous tests, they must be properly evaluated and correlated with other data.

The treatment is primarily *dermatologic.* The only approach from an allergic standpoint is the elimination of the causal agents. This is easy in some instances, difficult in others and in still others, unfortunately, impossible.

Desensitization is generally ineffectual, except possibly in cases in which the condition is due to plant oils.

The author finally points out that contact with the excitants need not necessarily be from without; it may be from within, providing the causal allergens reach the specifically sensitive shock tissue (epidermis?) in sufficient quantities (concentration) per unit of time and per size of area of skin. Cases of eczematous eruptions in which the condition appears after the injection or ingestion of quinine, methenamine, arsenicals or plant excitants are a few of many possible examples.

SYMPOSIUM ON ALLERGIC DERMATOSES: ALLERGIC DRUG ERUPTIONS. ADOLPH B. LOVEMAN, J. Allergy **11**:48 (Nov.) 1939.

A broad classification of drug eruptions would include all eruptions caused by drugs. The author limited the discussion to dermatitis medicamentosa—eruptions produced by the absorption and hematogenous spread of a drug or its split product. This absorption may result from ingestion, injection, inunction or even inhalation. Any drug, natural or synthetic, may produce a cutaneous or mucosal

hypersensitivity in some persons. There is considerable clinical and experimental evidence for judging dermatitis medicamentosa to be a manifestation of allergy.

The elicitation of the cutaneous response is not necessarily related to the amount of drug taken. Infinitesimal amounts of the drug may produce a cutaneous response, whereas, occasionally, tremendous doses of the drug may fail to produce an eruption in a person known to possess cutaneous hypersensitivity. Unquestionably, however, the extent, character and intensity of the eruption are related to the size of the dose.

Drug eruptions may appear days, months or even years after contact with the drug. On the other hand, an eruption may persist months, days or years after discontinuance of the use of the drug.

All drug eruptions, irrespective of their appearance, have characteristics in common. They appear suddenly, as a rule are bright red and have an atypically symmetric distribution, and the course is usually afebrile. Often they are accompanied by lesions on the mucous membrane, and, as a rule, the symptoms are mild.

The skin or mucous membrane are not the sole recipients of drug insults. Nerve pain, agranulocytosis, jaundice and headache have been observed after the ingestion of drugs. The author states the belief that many heretofore unknown visceral complaints may also be of drug origin.

SYMPOSIUM ON ALLERGIC DERMATOSES: ALLERGIC REACTIONS TO PLANTS. BEDFORD SHELMIRE, J. Allergy **11**:56 (Nov.) 1939.

Flowers, vegetables and weeds produce more or less distinct clinical types of eruptions. Sensitization to flowers and shrubs has been observed by the author chiefly in housewives and occasionally in florists. The most frequent eruption has been of the recurrent, vesicular type, usually confined to the hands, forearms, face and neck. Flowers such as the shasta daisy, chrysanthemum, narcissus, iris and carnation have produced acute dermatitis of the severity of an ivy or primrose eruption.

Sensitization to vegetables and fruits has been of both the acute and the chronic type. It has occurred in housewives, grocery clerks and truck gardeners. The eruptions have been almost universally confined to the hands. The author observed contact dermatitis from spinach, tomatoes, radishes, mustard greens, corn, Irish potatoes, oranges, lemons, grapes and other fruits and vegetables.

Dermatitis from weeds usually involves all the exposed areas, face, neck, hands, forearms, ankles and legs. Vesiculation and swelling are only rarely encountered. Lichenification of the flexures is an outstanding characteristic of eczema due to weeds. The eruption is at first seasonally recurrent, but eventually it becomes perennial. Clinically these chronic conditions closely resemble generalized neurodermatitis. Those usually affected are farmers and farmwives, oil field workers, members of surveyor and construction gangs and others.

Weed-sensitive persons present a polyvalent sensitivity; they should be tested with all the common weeds in their environment. The fresh leaf, portions of the dried plant and the extracted oleoresin may be used for patch tests.

Oleoresins are the best testing material. The author describes his method of preparing oleoresins, which is extracting with ether and acetone.

Best results of treatment have been in persons who have avoided further contact with weeds. Hyposensitization by intramuscular injection or ingestion of the antigenic oils gave poor results. Some patients, however, felt that they have either been desensitized or greatly benefited by the oral administration of the antigenic oleoresins.

SYMPOSIUM ON ALLERGIC DERMATOSES: INFANTILE ECZEMA. RUDOLPH HECHT, J. Allergy **11**:195 (Jan.) 1940.

Infantile eczema is not a well defined condition. Hill has subclassified the group into seborrheic dermatitis, contact dermatitis, eczematous fungous eruptions and atopic dermatitis. Any one or more of these may be present in the same

person, and one form may be transformed into another. The differentiation of the various types from one another is sometimes impossible.

The diagnosis of infantile atopic dermatitis is based on a family history of atopy, the presence of immediate wheal type reactions to scratch or intracutaneous tests with the usual atopens, negative results to patch tests with contact substances, the presence of reagins in the serum and eosinophilia. Morphologically, there is an erythematous, papulourticarial, vesicular, frequently weeping eruption usually occurring on the face and neck and accompanied by violent uncontrollable itching.

Environmental substances, such as house dust and feathers, play a significant role in infantile eczema. The removal of these substances plus elimination of certain foods offer better results than just the elimination of certain foods. The best method of treatment is careful dermatologic management, including proper choice, application and removal of local remedies, bandaging, careful splinting to prevent scratching, avoidance of soap, the use of sedatives and general hygienic and medical care.

SYMPOSIUM ON ALLERGIC DERMATOSES: ATOPIC DERMATITIS. BEN Z. RAPPAPORT, J. Allergy **11**:200 (Jan.) 1940.

The morphologic characteristics of the childhood and adult types of atopic dermatitis differ from those of the infantile type. The former types merge, one into the other, morphologically. The lesions are no longer vesicular and develop in definite areas of predilection: the forehead, scalp, sides of the neck, the wrists and the flexures of the elbows and knees.

In a large proportion of cases the condition clears with or without treatment at the age of 2 years, with no recurrences. In others, there is a recurrence at about the age of 5 to 7 years. After months or years the condition clears up in some, either permanently or with recurrences at puberty. If there are recurrences at puberty the condition lasts until the patients are in their twenties or thirties, when, with or without treatment, it clears in most patients.

There is a definite seasonal occurrence or flare-up in many cases. A large group of patients are worse in the winter, and in others the symptoms develop at the beginning or at the height of the various pollen seasons. The majority of patients in the latter group have concomitant symptoms of hay fever.

Some of the cases occurring during the summer have shown definite improvement after pollen hyposensitization. The results of such treatment, however, have not been uniform in the hands of the author.

Foods as a cause of atopic dermatitis are more important in the child than in the adult. The importance of the immediate wheal type of reaction with various atopens is controversial. The author found them of greater value in children than in adults. The most practical approach for adults is to place the patient in a carefully controlled environment, with unusual care in the way of dust-free precautions, and then to treat the condition by topical means. Elimination diet studies are of importance, primarily in childhood.

It is strange to see a patient improve rapidly in a hospital room and then, with practically identical furniture and food at home, suffer a relapse, only to improve again on hospitalization. There may be many atopens in the home that have not been recognized as causes of trouble.

SYMPOSIUM ON ALLERGIC DERMATOSES: FUNGUS ALLERGY. SAMUEL M. PECK, J. Allergy **11**:309 (March) 1940.

The same organism, whether a bacterium or a fungus, can give rise to totally different syndromes, while unrelated pathogens can initiate practically identical pictures. Eruptions due to micro-organisms can be divided into two classic types: (1) typical forms, which are due to fungi themselves, and (2) atypical forms, referred to as cutaneous microbids. The latter depend for their development on

the interaction between bacteria and fungi, or their products, and the allergic skin. Tuberculids, trichophytids and levurids are classic examples of cutaneous microbids.

The epidermophyton and trichophyton fungi grow in the nonliving layers of the skin and its appendages. Inflammatory reactions do not develop until the living structures are involved, when hypersensitivity with its resulting allergic manifestation is brought about. This sensitivity is revealed by a positive trichophytin reaction which is specific for the group in the majority of instances. The period between onset of infection and development of hypersensitivity varies from a few months to several years.

Continuous maceration, trauma, application of strong ointments or even roentgen rays force the fungi or their products into the blood stream. These in turn, coming in contact with the hypersensitive skin, give rise to trichophytids.

The diagnosis of microbids is made with great frequency and often without proper supporting evidence. The author lists criteria for the establishment of such a diagnosis. An instructive classification of trichophytids is included.

The reaction to the trichophytin test is not always the same in degree throughout the year. The author found that the reactions were more strongly positive during periods of exacerbation of the primary focus. False positive reactions are often due to secondary bacterial contamination or to the ingredients of the mediums themselves.

The immediate reaction to trichophytin is rare; patients manifesting such reactions usually do not have the delayed type of reaction.

The reaction after injections of oidiomycin is positive in practically 100 per cent of adults, but in infants and young children positive reactions are rare.

The results of use of trichophytin as a therapeutic measure were disappointing. Recently, however, the author observed improvement of patients with trichophytids by the injection of trichophytin.

SYMPOSIUM ON ALLERGIC DERMATOSES: ALLERGIC OCCUPATIONAL DERMATOSES. LOUIS SCHWARTZ, J. Allergy **11**:318 (March) 1940.

Many cases of occupational dermatoses seemingly due to allergy can be explained by changes in working conditions, by variations from the normal in the skin of the worker or by breaks in the defense mechanism of his skin. In a compilation of about 10,000 cases of occupational dermatoses made from the reports of various state compensation boards, allergy was the cause of the dermatoses in less than 18 per cent of the cases.

In allergic occupational dermatitis, the period of incubation is usually eight to twenty-one days, although it may be longer. A dermatitis which develops in less than a week after exposure to an irritant is usually not due to allergy acquired from that particular job. On the other hand, a worker may get an allergic occupational dermatitis even three weeks after leaving a job in which he was exposed to sensitizers.

The patch test gives a rapid, although not altogether reliable, clue as to the allergic origin of an occupational dermatitis. If the dermatitis was or is generalized and the reaction to patch tests with great dilutions of chemical spreads, if the dermatitis—if still present—becomes exacerbated as a result of the patch test, if areas of healed dermatitis light up anew or if new areas of dermatitis develop and constitutional symptoms follow the application of the patch test, then allergy is probably present.

The author includes a list of chemicals which he found to produce allergic occupational dermatitis. Some chemicals, such as the chromates, many essential oils and insecticides, are primary irritants in strong concentrations and sensitizers as well. Allergy to finished dyes, so often seen among the wearers of dyed clothing, is not common among the workers engaged in manufacture of dyes.

Spontaneous desensitization may occur in industry. Occupational exposure first causes a sensitivity, and then, after the exposure continues, an immunity develops

in some cases—the workers become "hardened." Workers in whom such an immunity does not develop should be transferred to other occupations.

Attempts to desensitize by giving minute increasing doses of the sensitizing agent have met with success in only a few isolated cases.

MENDELSOHN, New York.

DERMATOLOGY AND FOLK-LORE. J. D. ROLLESTON, Brit. J. Dermat. **52**:43 (Feb.) 1940.

Aside from being of interest, this article is an excellent source of material for those interested in medical folklore.

PSORIASIFORM CARCINOMA OF THE PENIS. LOUIS SAVATARD, Brit. J. Dermat. **52**:87 (March) 1940.

Savatard includes under the title psoriasiform carcinoma lesions of erythroplasia of Queyrat, Paget's carcinoma and Bowen's disease. There is some variation in the clinical appearance of these lesions, just as there may be in psoriasis; the color may be bright red, pink, dull red, brownish red or even brown. The diagnosis is made by histologic examination. The term "psoriasiform" is merely descriptive of the clinical picture, in the same sense that the term "morphea-like" is used in "morphea-like epithelioma."

ENVIRONMENT AND SKIN DISEASE. F. F. HELLIER, Brit. J. Dermat. **52**:107 (April) 1940.

This paper presents an analysis of figures based on patients attending the dermatologic department of the General Infirmary at Leeds, with particular attention given to the effect of climatic changes on the incidence of various cutaneous diseases. The patients were from an industrial town of half a million inhabitants, employed in many different trades, including the manufacture of iron and steel, coal mining, printing and all the processes associated with the manufacture of cloth.

The incidence of eczematous eruptions, including both exogenous dermatitis and constitutional dermatitis, when studied with respect to monthly incidence in the community was found to be remarkably constant, but there was a high incidence of industrial dermatitis.

Infantile dermatitis, on the other hand, showed peaks in the spring and autumn, and in an effort to explain these peaks the figures were studied with respect to barometric pressure, wind, cold and other factors, because infants are least exposed to the influence of external irritants. There was not an accurate correspondence between the months with the lowest barometer readings and those with the highest incidence of eczema, nor was severity of cold an important factor in the variations from year to year in the incidence of infantile eczema. No relation could be found between eczema and the relative humidity, though, if anything, the wetter springs were associated with a somewhat greater incidence of eczema; there was a slight decrease of incidence with a higher drier temperature.

Hellier concludes, however, that these factors, although not fundamental factors in infantile eczema, may play a small part in that during the spring months they are all acting in the same direction. In the spring there is an increase of irritability of the skin completely independent of any direct action of external factors. This increased reactivity occurs with other changes in the spring, such as increased sexual activity, and these are part of the rhythm found throughout the whole animal kingdom.

Urticaria had its great frequency in autumn, but there were not enough data to permit the drawing of any conclusions. Psoriasis seemed definitely to be influenced by the number of hours of sunshine, and the figures indicated that the influence of the sunshine on the skin operates for a considerable time after

exposure. Rosacea showed a definite association with cold weather. Other diseases, such as scabies, lichen planus, carcinoma and impetigo, were investigated with respect to their relative incidence and were not studied from the viewpoint of the effect of environment on them. RATTNER, Chicago.

THE LOCAL TREATMENT OF ULCERATED ORIENTAL SORE BY THE POWDER OF CERTAIN SULPHONAMIDE DERIVATIVES. F. AKRAWI, J. Trop. Med. & Hyg. **43**:4 (Jan.) 1940.

Baghdad, Iraq, is the largest endemic center for oriental sore in the world. The ulcerated phase of the disease offers a difficult therapeutic problem. Local treatment by paints and ointments is unsatisfactory in most cases. Physical agents, such as cauterization, coagulation and application of solid carbon dioxide, frequently give rise to keloids. Solid carbon dioxide, however, is the best of the three aforementioned treatments. Roentgen ray therapy is to be recommended. The authors state that the internal administration of an antimony preparation produces but a small percentage of cures. The author treated the ulcerated forms of the disease by means of sulfanilamide and sulfapyridine powder. After the lesion was cleansed with saline solution, the powder was applied daily until complete healing was obtained. If the period of treatment exceeded one month the treatment was discontinued, and the case was registered as unsuccessful. Absolute cure took place in less than one month in 63 per cent of the author's cases, an unusually short time for ulcerated Baghdad boils. LAYMON, Minneapolis.

Society Transactions

CHICAGO DERMATOLOGICAL SOCIETY

HERBERT RATTNER, M.D., *President*

M. H. EBERT, M.D., *Secretary*

April 17, 1940

Keratosis Follicularis (Darier). Presented by DR. N. C. BARWASSER (by invitation) and DR. E. B. RITCHIE (by invitation), Davenport, Iowa..

W. L., a married white man aged 37, states that the eruption first began when he was 5 years old, on the hands and neck. When he was 21, the condition had become generalized. On three occasions he has had acute flare-ups involving the face and the scalp, with swelling of the glands of the neck.

He has had pneumonia twice within the past twelve years, and during these attacks the cutaneous condition improved. A corneal opacity of the right eye developed ten years ago following an injury.

The family history reveals a strain of mental instability, selecting the male side of the family. One older brother has Parkinson's disease. The mother and three sisters are living and well.

The eruption consists of brownish follicular keratotic papules, which average 44 mm. in diameter, of almost universal distribution, more confluent toward the middle portions of the body. There is a background of dusky erythema particularly noticeable on the face. The legs are encased in a mass of heaped-up dry, tightly adherent scales. On the palms and soles there are well defined areas of keratosis. On the mucous membrane of the hard palate there is a diffuse whitish verrucous patch.

Laboratory examinations revealed nothing of significance except a leukocyte count of 8,300 per cubic millimeter, with 8 per cent eosinophils. The biopsy specimen showed the histologic picture of Darier's disease.

Treatment has consisted of about forty-five intravenous injections of gold and sodium thiosulfate, with an average of 30 mg. per dose. Both grenz rays and roentgen rays have been used on selected areas on the legs.

A Case for Diagnosis (Keratosis Follicularis [Darier]?). Presented by DR. THEODORE CORNBLEET.

J. D., a white man aged 21, presents an eruption on the back, shoulders and neck of two years' duration. The condition is not very pruritic. The lesions consist of light red papules, varying in size from that of a pin to that of a match head. They have a tendency toward follicular involvement and some are verrucous.

DISCUSSION

DR. C. W. FINNERUD: Both patients show unusual examples of Darier's disease. One has probably the most extensive condition that has ever been seen. Dr. Cornbleet's case should be studied histologically to make the diagnosis certain.

DR. E. B. RITCHIE (by invitation), Davenport, Iowa: An interesting feature in the family history of the first patient is that his younger brother has Parkinson's disease, indicating a possible familial ectodermal defect.

DR. DAVID LIEBERTHAL: The subsequent history of a patient I reported on in 1904 (Lieberthal, D.: A Case of Darier's Disease, *J. A. M. A.* **43**:242 [July 23] 1904) disclosed that several cases of a similar condition of the skin occurred in three generations of his family.

A Case for Diagnosis (Congenital Dyskeratosis and Leukokeratosis Oris?). Presented by Dr. N. C. Barwasser (by invitation) and Dr. E. B. Ritchie (by invitation), Davenport, Iowa.

E. Y., an unmarried white man aged 23, born of Slavic parents, is by occupation a miner. There is nothing of significance in his medical history or in the family history. He graduated from high school at the age of 19.

He had warty lesions about the eyes and lips at birth. When he was 3 years old the lower lip became so pendulous that it required a surgical operation. Hoarseness has been present since early childhood. Two years after a tonsillectomy, when he was 11 years old, changes were first noticed in the mouth. When he was 12 years old warty lesions appeared on the backs of the hands. Since then the legs, arms, feet, lumbar vertebral region and gluteal folds have become involved. Bullae are said to have occurred through this progression, although not definitely related to trauma.

The patient presents a dry vegetative flesh-colored dermatosis involving the upper and lower eyelids, producing a well defined rim measuring 4 mm. in width and 2 mm. in elevation. There is some thickening about the nares. The lips are thickened and show the same type of vegetative process, which blends gradually with the skin of the circumoral region. In the glabellar region there is a less well defined area of smooth hypertrophic change. A small soft flesh-colored nodule is present on the helix of each ear. The mucous membranes of the mouth are thickened, whitish and coarsely verrucous. The tongue is small and hard and limited in movement. There are leukokeratotic changes over the entire tongue. The teeth are in advanced stages of caries, widely spaced and peg shaped. On the extensor surfaces of the elbows, forearms and knees, the tibial aspects of the legs, the dorsa of the feet, the lumbar vertebral region and the gluteal folds, extending down to and surrounding the anus, are variously sized, discrete and confluent, dry hypertrophic plaques, showing scaling and slight erythema. Within these areas are many acutely inflamed lesions with necrotic centers. There are also faint cribriform atrophic lesions of various sizes both within these hypertrophic areas and elsewhere, noticeably on the flexor surfaces of the forearms. On the dorsa of the feet and hands, as well as on the palms and soles, there are discrete areas of dry, brownish, sharply pointed, verrucous lesions.

The nails of the fingers and toes are normal. The body hair shows no abnormality. There is no hyperhidrosis.

The Kahn test gave a negative reaction. The red blood cell count was 4,600,000 per cubic millimeter, with 90 per cent hemoglobin, and the white blood cell count was 6,800 per cubic millimeter, with a normal differential count.

The biopsy specimen taken from the back of the hand showed the epithelial surface to be thrown into sharp pointed folds. There was intense hyperkeratosis, thickening of the stratum granulosum and acanthosis, with some intercellular edema. There was round cell infiltration scattered throughout the upper portion of the corium. The blood vessels showed some dilatation.

DISCUSSION

Dr. Ruben Nomland, Iowa City: I saw this man several months ago. After looking up the literature I thought that he presented a syndrome of ectodermal defect, as in cases of pachyonychia congenita recently described. He has much less involvement of the nails than in most cases of this disorder, but it is like a good many that have been described. It is also like the case that Dr. Cole (Arch. Dermat. & Syph. **21**:71 [Jan.] 1930) described, in which he differentiated between these ectodermal defects.

Dr. M. H. Ebert: In looking at the mouth of this patient with Dr. Wile, we both noticed the resemblance between the lesions in the mouth and on the tongue and the lesions in a case of amyloidosis that was presented at the meeting in Ann Arbor. The rest of the syndrome showed no resemblance. It is possible that in these lesions amyloid might be demonstrated.

DR. N. C. BARWASSER (by invitation): I am indebted to Dr. Nomland for some fine pictures and also for his opinion on this case. One feature that impressed me is that there were no apparent changes in the nails.

Atrophia Pilorum. Presented by DR. E. E. STENHOUSE (by invitation).

Miss M. E., a stenographer aged 24, states that the hair of the scalp was normal until she was 14 years of age. At that time she noticed two areas on the vertex in which the hair became thin and short. At no time were the areas bald. Hair gradually grew in these areas again, but it was short and thinner than before.

When she was first seen in September 1938, there were several small areas in which the hair was short (from 1 to 2 inches [2.5 to 5 cm.]), coarse and dry. These areas gradually enlarged, until now there is short fine hair over the entire scalp except about the ears and at the nape of the neck. The hair in the involved areas now seems to be of more normal texture but finer and thinner. At no time has there been inflammation or evidence of disease of the hair, bulb or shaft. There is no splitting at the end of the hair. The hair on the other parts of the body is normal.

About two months ago the finger nails became pitted to such an extent that the pits appeared to be in transverse ridges.

Her general health is good. Her only complaint is fatigue after a day's work. The serologic examination of the blood gave negative results; the urine was normal. There is a mild grade of secondary anemia. The basal metabolic rate last week was —24 per cent.

Treatment has included local treatment of the scalp, administration of thyroid, of vitamins and of hematinics and ultraviolet irradiation.

Atrophia Pilorum. Presented by DR. S. W. BECKER and DR. M. E. OBERMAYER.

Miss E. J. was first seen in July 1935, at the age of 19, complaining of partial loss of hair of four years' duration. The alterations took place in about two months, during which time the hair over the vertex tended to fall out more freely than normally, and new hair in that region was short, about 2 cm. in length. The hair at the inferior portions of the scalp and in the nuchal region retained its normal length.

Various methods of therapy have been used, with no improvement. Physical examination showed no abnormalities. The Kolmer and Kahn reactions of the blood serum were negative. There is no history of a similar condition in the family.

Microscopic examination of the hair showed it to be atrophic, but there were none of the signs characteristic for monilethrix or trichorrhexis.

DISCUSSION

DR. S. W. BECKER: When we first saw this patient some years ago I tried unsuccessfully to find a similar condition in the literature. It is striking that this young girl retains normal hair at the fringe, as do some bald men. The condition is not premature alopecia, because the hair is present over the vertex, but it is atrophic and persists in its atrophic state.

Pyoderma Faciale. Presented by DR. HERBERT RATTNER and DR. THEODORE CORNBLEET.

Miss E. H., a white American aged 30, states that she had no trouble with her skin until six or seven years ago, when occasionally pimples appeared on her face. There were not enough for her to seek medical attention until about a year ago, when the condition became suddenly worse. With ointments and ultraviolet ray therapy during the summer and fall of 1939 the condition improved. In January 1940 there was an exacerbation, for which she again received treatment with ultra-

violet rays and a liquid medicine, which, according to her physician, contained ferrous sulfate, diluted sulfuric acid, potassium sulfate, magnesium sulfate and water. New lesions continued to develop, and for the past two months she has been forced to give up her employment. She has not taken any iodides or bromides. Her menstrual periods have been regular, every twenty-eight days, without dysmenorrhea. Aside from a nervous breakdown and gastrointestinal complaints when she was 20, she has always been in good health.

The physical examination showed no abnormalities. A number of teeth have silver fillings. The skin of the forehead, cheeks, nose and chin shows cyanotic erythema with some puffiness. The skin around the eyes is normal. The involved portions are composed of superficial and deep abscesses and cystic lesions which seem to communicate with one another. The surface is studded with pustules of various sizes, especially around the mouth and chin, and dried honey-colored crusts are scattered about the surface of the lesions. Pitted scars are visible on the cheeks. Isolated pustules and cystic lesions are scattered on the neck and the central area of the chest. No comedos are seen.

Laboratory Tests.—The urine was normal. Examination of the blood showed: 78 per cent hemoglobin and 4,150,000 erythrocytes and 13,650 leukocytes, per cubic millimeter, with 77 per cent polymorphonuclear leukocytes, 2 per cent eosinophils, 16 per cent lymphocytes and 5 per cent monocytes. The basal metabolic rate was —5 per cent. A roentgenogram of the chest showed no pulmonary changes. A Mantoux test, with a dilution of 1:10,000 of old tuberculin gave a positive result. The Kahn test gave a negative reaction.

DISCUSSION

DR. PAUL A. O'LEARY, Rochester, Minn.: This condition is typical of the eruptions Dr. Kierland and I recently described as pyoderma faciale (ARCH. DERMAT. & SYPH. **41**:451-462 [March] 1940). The disease is characterized by an explosive eruption on the face of women in their early twenties who have not had preceding acne. The characteristic lesion is the deep pustule, with subsequent development of tunnelling abscesses and resulting keloid. Comedos, not only on the face but also on the chest, are conspicuous by their absence. These patients are underweight and anemic and frequently have amenorrhea. Efforts to attribute the eruption to a focus of latent tuberculosis elsewhere in the body have failed. Histologic section, tuberculin tests and guinea pig inoculations have not thrown any light on the problem. The point that Dr. Kierland and I endeavored to stress is that the therapeutic program should be mainly directed to the patient's systemic status, giving treatment for the anemia or amenorrhea and prescribing rest in bed and high vitamin diet. The local measures of draining the abscesses, roentgen ray irradiation for the keloidal scarring and application of a mild sulfur preparation should be carried out simultaneously. The explosive onset of the eruption in a person who has not had acne vulgaris and who manifests few comedos characterizes the disease.

DR. FRANCIS E. SENEAR: Dr. O'Leary not only has given a good description but has given the condition a name. The condition in these cases does not fit any other particular description of acne. I for one am glad to have a name for cases of this type.

I should like to ask Dr. O'Leary if this condition occurs in persons of the rosacea age. Most of the examples I have encountered have occurred in a much younger age group.

DR. S. W. BECKER: I have had a few cases. The facts that the condition occurs in patients of the rosacea age and resembles rosacea led me to think that it was simply a severe form of rosacea. Treatment has been the same as Dr. O'Leary's, sunshine and rest, which results in great improvement.

DR. H. E. MICHELSON, Minneapolis: I still feel that this condition belongs to the acne group. I have seen it, of course, many times and I believe that when the pustules are opened comedos can be found in the pus. Although some patients do not respond to the treatment employed for acne, many do.

DR. HERBERT RATTNER: I can recall having encountered several such eruptions that belong, I think, in the group of pyoderma faciale. I did not know where to classify them, for the condition differed from ordinary severe acne, and certainly it was not an example of rosacea.

Generalized Scleroderma. Presented by DR. HERBERT RATTNER and DR. THEODORE CORNBLEET.

Mrs. B. T., a Negress aged 39, was well until about two years ago, when she started to vomit an hour or so after meals. There was no pain. At the same time she noticed an increased pigmentation of the skin, especially of the neck and face, which gradually involved the entire surface of the body. In time the pigmentation became lighter, so that the skin became depigmented and mottled, first on the neck, face and chest and later on the extremities. About eighteen months ago, her hands commenced to swell, the condition lasting a few weeks, after which the skin remained tense and shiny with restricted motion of the fingers. Recently she has noticed decreased ability of the jaws to move and inability to protrude the tongue beyond the lips. There has been a gradual loss of hair from the scalp. Her appetite has remained good, but she has lost 40 pounds (18 Kg.) in the last two years, with a loss of strength. She also complained of coldness and numbness of the extremities.

The patient has had four pregnancies. The first occurred when she was 16, and she bore a full term normal child, who is now 24 years of age. The next three pregnancies resulted in spontaneous miscarriages at four months, with considerable loss of blood each time. Her menstrual periods have occured regularly every twenty-eight days, even through the present condition.

Her father and mother are living and well, aged 80 and 73 years, respectively, as are two sisters and four brothers. There is no similar disease in the family.

Physical examination reveals a somewhat emaciated Negress with sparse hair on the scalp and a masklike expression on the face. The neck has a mottled appearance, with light linear streaks running perpendicularly on the anterior surface. All the skin of the body is hidebound, rigid, shrunken and atrophic, with a glossy sheen, especially over the extremities. Pigment is retained about the follicles, giving a dotted appearance to the skin.

Laboratory Tests.—The urine was normal. The Kahn reaction was negative. The basal metabolic rate was —3 per cent. The cholesterol content of the blood amounted to 219 mg., the calcium to 8.46 mg. and the phosphorus to 4 mg. per hundred cubic centimeters. The nonprotein nitrogen, creatinine and sugar contents of the blood were within normal limits. Roentgenograms of the chest, the bones of the right hand and the gastrointestinal tract were normal. The histologic picture was compatible with the diagnosis of scleroderma.

DISCUSSION

DR. S. W. BECKER: This patient presents an interesting course of events from the standpoint of pigmentary disturbance. In the first place she was a rather light-skinned Negress. Then she became dark over most of the body; later she became depigmented, and at present she is regaining pigment, first of all between the follicular orifices. Dr. Oliver called my attention to the fact that Negroes become depigmented with the use of rubber gloves. This loss of pigment between the follicles, with pigment returning first of all in the follicles, suggests that in some of these conditions the follicular pigment is the last to be lost.

DR. E. A. OLIVER: An interesting feature in these cases of depigmentation is the behavior of the pigment in the hair follicles. It is the last to disappear and the first to reappear. Another peculiar thing in the group of cases of leukoderma was that the hairs remained unaffected; none of them were depigmented. More will be learned about pigment formation as unusual cases are encountered.

In examining sections, Dr. Weidman found that the cells of the granular layer of the epidermis gave dopa reactions and that there were dopa-positive granules in the stratum corneum and in the secretory cells of the sweat glands.

DR. HERBERT RATTNER: This patient has shown considerable improvement both in general well-being and in the cutaneous lesions from treatment with histamine induced by iontophoresis.

NOTE.—The patient subsequently died of pneumonia.

A Case for Diagnosis (Infectious Dermatitis?). Presented by DR. M. H. EBERT.

M. B., a white woman aged 50, presents an eruption on the dorsum of the left forearm and left wrist and on the right leg near the knee. About seven months ago the first lesions appeared as moderately itchy papules on the dorsum of the left hand. About four months ago similar lesions appeared on the areas involved at present. The lesions spread peripherally and cleared centrally.

The lesions are gyrate and appear to have been formed by the coalescence of coin-sized annular lesions. A threadlike, raised margin, 1 to 2 mm. across, is made up of vesicopapules which have coalesced. The central area is slightly hyperpigmented but not atrophied.

Histologic examination showed the following picture: Most of the stratum corneum had been exfoliated. The remaining lamellas were parakeratotic. The stratum granulosum was absent. The rete mucosae was acanthotic. There was intercellular and intracellular edema. In places there was decided migration of the leukocytes through the rete, with the formation of microabscesses in the upper part of the rete. The upper part of the corium was edematous. A slight perivascular round cell infiltrate was present.

DISCUSSION

DR. C. W. FINNERUD: I do not know what the eruption is, but I believe it probably fits in better with erythema annulare centrifugum than with anything else, after considering the clinical and histologic observations. I feel rather strongly that the condition is not psoriasis or lichen planus.

DR. M. R. CARO: I thought that histologically most of the conditions mentioned could be ruled out except psoriasis. There were certain changes, like microabscesses and changes in the papillae, that would suggest psoriasis.

DR. M. H. EBERT: This case has been rather confusing. When I first saw the patient the lesions were dry, with little scaling and with a threadlike border. I concluded that clinically the disease was erythema annulare centrifugum. On looking at the sections I was struck by the presence of microabscesses and also of microscopic vesicle formation, as well as by the great amount of acanthosis, more than one would expect in psoriasis. The next time I saw the patient, which was two days ago, the clinical appearance bore out the impression gained from the histologic section in that there were tiny vesicles present in this border. Two days later they began to disappear. In two or three weeks little spread has occurred; so the condition could not be called erythema annulare centrifugum unless it is just starting. I did think of infectious dermatitis with a centrifugal spread. Examinations were made for fungi, but none were found.

Psoriasis with Pustular Exacerbation. Presented by DR. DAVID V. OMENS and DR. WALTER W. TOBIN (by invitation).

K. B., a woman aged 52, states that six months ago a red, itchy eruption appeared on her thighs, beneath the breasts, about her ears and on the feet, hands and arms. It became progressively more severe, necessitating hospitalization. Within the past three weeks, and since she left the hospital, the eruption has become worse.

The past history is essentially not significant.

Examination discloses diffuse erythematous, crusted dermatitis on the upper, inner parts of the thighs, in the groins, beneath the breasts, about the face and ears and on the forearms. There are numerous small discrete abscesses in the aforementioned areas and especially on the dorsa of the hands, toes, forearms and knees and about her ears.

The blood and urine were normal. Biopsy of a pustular lesion showed typical psoriatic changes with a large epidermal pustule and a lymphocytic infiltrate in the corium below it.

DISCUSSION

DR. HARRY R. FOERSTER, Milwaukee: I believe that the condition may be moniliasis in a patient with psoriasis, because of the type of lesion in the non-intertriginous areas. The changes in the nails are suggestive of psoriasis, and the lesions under the breasts, while suggesting moniliasis, have features that psoriasis may exhibit in such localities. The lesions in flexural areas are more infiltrated than typical monilial eruptions. The fissured lesions at the corners of the mouth are the only ones that cannot be explained in a diagnosis of psoriasis.

DR. DAVID V. OMENS: This patient was in the hospital three or four months ago, and at that time she presented a similar picture, but the condition was not as pustular as it is now. At that time the resident made a microscopic examination and found Monilia. She was treated with dressings soaked in potassium permanganate solution and seemed to do well. I saw her two days ago for the second time, and she had an acute exacerbation. The first time she presented diffuse pustules in these patches. She shows considerable change in so short a time, e. g., two days.

DR. OLIVER S. ORMSBY: Some years ago Ebert (Ebert, M. H.: A Psoriasiform Eruption with Pustular Exacerbation, ARCH. DERMAT. & SYPH. **27**:933 [June] 1933) reported on 2 patients (sisters) who had been under my observation for a number of years. The first patient had had recurrent attacks of some cutaneous condition since infancy. When she was 12 years old psoriasiform lesions developed on the elbows, trunk and scalp. Later the lesions on the scalp became pustular, and a general exfoliative dermatitis supervened, lasting a year and a half. During my observation of this case, which included several periods in the hospital, the disease ran a varied course. When it was comparatively quiescent, plaques of ordinary psoriasis were present on the extensor surface of the arms and on the back and legs, and there were scaling lesions on the scalp. During an active attack the plaques became acutely inflamed and were surrounded by an areola, with the development of numerous pustules. The plaques increased in number and were found in the usual areas of psoriasis. The inflammatory areola was often beset with numerous minute intradermic pustules, and the lesions felt hot and were tender. All the nails were involved. During an acute attack the temperature became elevated, and there was leukocytosis (15,000 leukocytes per cubic millimeter).

In the height of an attack the eruption became extensive and presented numerous flat pustules generally distributed, together with much cutaneous edema. After ten days the acute phase subsided, leaving only psoriasiform plaques.

An exactly similar condition existed in the patient's sister, which consisted of recurring attacks, which at times developed into general exfoliative dermatitis with psoriasiform plaques in the quiescent stage and pustular lesions together with lesions of infectious dermatitis in the more active phases.

Pustular psoriasis of Barber, which is largely limited to the hands and feet, is different from the condition in the cases described and in the case shown today. Dermatitis seborrhoeica and a mycotic (yeast) infection should be considered in this case. A period of observation may show definitely that the condition is psoriasis with pustular exacerbation.

DR. DAVID V. OMENS: We have not given her sulfathiazole. We have given her sulfanilamide but not enough as yet to obtain results.

A Case for Diagnosis (Gangrene? Toxic Eruption?). Presented by Dr. Herbert Rattner and Dr. Irene Neuhauser (by invitation).

R. B., a white woman aged 41, was admitted to the hospital two weeks ago. She states that immediately prior to her illness she had been well and that one week before admission she noticed that her nose was beginning to swell, the swelling gradually spreading over the upper portion of her face, causing her eyes to close. Also severe intermittent pain developed in her left leg, and there were redness and swelling of the lower third of the right leg.

In 1929 the patient was in Cook County Hospital with an illness which was apparently similar to the present one, swelling of the face and tongue, which resulted in gangrene and sloughing of the left ala nasi. Also necrosis developed in some of the small nodules which appeared on the lower extremities. At that time a diagnosis of erythema multiforme was made.

On admission this time the patient presented a deep-seated erythematous blush, with swelling over the nose and adjacent portions of the cheek. The tongue was swollen to several times its normal size. The tissues of the left ala nasi were missing. Symmetrically arranged on the thenar eminences were groups of deep-seated tender nodules. Later similar nodules appeared on both upper and lower extremities. Movement of the right wrist was difficult and painful.

At present the erythema and swelling of the face have disappeared, and an area of gangrene has developed, involving the right ala nasi and a small area in the labionasal fold. The swelling of the tongue has subsided, and an ulceration has appeared on the dorsum. The deep-seated, tender nodules on the thenar eminences and extremities are still present.

General physical examination revealed no adenopathy. The heart and lungs were essentially normal. Examination of the blood showed 4,000,000 erythrocytes and 28,650 leukocytes per cubic millimeter, with a normal differential count. Chemical examination of the urine revealed a 2 plus reaction for albumin and a trace of sugar. The microscopic examination showed a few erythrocytes and leukocytes and many granular casts.

Histologic examination showed that the epidermis was normal. There was a moderate degree of edema in the corium, with circumscribed mantles of infiltration about the blood vessels and sebaceous glands, consisting of loosely packed round cells. The biopsy specimen included but little subcutaneous fat, but it was here that the greatest inflammatory changes were seen, consisting of a diffuse infiltration of lymphocytes, histiocytes and a few plasma cells.

DISCUSSION

Dr. Max S. Wien: Dr. Finnerud and I saw this patient ten years ago in Cook County Hospital. At that time the diagnosis was erythema multiforme. She also had coin-sized patches on the trunk, compatible with a diagnosis of phenolphthalein eruption. Today she says she has not used any preparation in douches. This patient has erythema toxicum with severe local vascular allergy and associated necrosis, which may be produced by many different agents, such as drugs or infections.

Dr. C. W. Finnerud: The whole process apparently is much more marked than when I saw the patient ten years ago. She has lost most of the nose since then. The disease appears to me to be an infectious process of internal origin. It certainly does not look much like erythema multiforme now.

Dr. Paul A. O'Leary, Rochester, Minn.: The diagnosis of syphilis seems warranted. The tongue has the signs of syphilitic glossitis.

Dr. M. R. Caro: The biopsy specimen was taken from a lesion on the forearm. Unfortunately it cannot be of much help in making a diagnosis because most of the pathologic changes seem to lie deep in the fatty tissue, and the specimen was not cut deep enough to include them. The histologic picture, however, does not seem to be compatible with that of syphilis.

DR. DAVID LIEBERTHAL: I am strongly inclined to second the suggestion of Dr. O'Leary, to try antisyphilitic treatment in this case. I especially recommend using potassium iodide first.

DR. MINNIE PERLSTEIN: I saw this patient ten years ago when she had her first attack and again last week when she first entered the hospital. Ten years ago the picture was essentially the same as it is today except that the involvement was on the left side of the face. At that time she presented an involvement of the hands similar to that present today. On admission a week ago she presented an erysipelas-like swelling over the right cheek, extending from the angle of the mouth to the eyebrow, and she was acutely ill. A few days later painful erythematous plaques appeared diffusely scattered over the extremities, so that her legs could not be touched because of excruciating pain. Now she has no pain at all. The surprise to me now is to find that all the edema of the cheek has subsided and instead of a severe slough over the zygoma, which I believed would occur, there is but a small area of gangrene limited to the left ala nasi.

Lichen Planus Linearis. Presented by DR. M. H. EBERT.

P. V., a white girl aged 9 years, presents a linear eruption along the course of the left sciatic nerve. This appeared suddenly four weeks ago and does not itch. The lesion consists of a band 1 cm. wide made up of closely aggregated pinhead-sized flat papules, which were bright red when first seen.

Histologic examination showed: (*1*) lamellar hyperkeratosis; (*2*) hypergranulosis; (*3*) acanthosis; (*4*) edema of the rete, with fraying out of the lower cells into the infiltrate of the corium; (*5*) edema of the papillary layer, and (*6*) fairly well defined round cell infiltration of the papillary and subpapillary layers.

DISCUSSION

DR. FRANCIS E. SENEAR: This case is one of those which Dr. Caro and I have recently been interested in. We have presented a number of cases before the society. Those we have been interested in recently have not been of lichen planus. There is often a great deal of difficulty in differentiating clinically lichen striatus from linear lichen planus. In this particular case, from a clinical standpoint, with the light just right one can see some lesions which are lichenoid in character, flattened, annular and brownish. In situations of that type I would say that the diagnosis ultimately has to rest on the microscopic picture. A point in favor of lichen striatus rather than lichen planus is that this condition has appeared and largely disappeared in six weeks' time. All authors point out that in dermatoses, such as lichen planus and psoriasis, the linear forms are more chronic. It has been our experience with the 8 cases of lichen striatus which we have had the opportunity to study that spontaneous involution in a period of a few weeks to a few months has been characteristic. In this particular case there is nothing in the clinical picture which might not be part of a slightly modified lichen planus.

DR. C. W. FINNERUD: I felt that the case histologically was one of lichen planus. There was hyperkeratosis, and a well defined infiltrate was present in one part of the section. Dr. Oppenheim did not think the condition could be lichen planus, because there was no sharp demarcation between the infiltrate and the basal layer of the epidermis. In my experience that very feature speaks for lichen planus rather than against it.

DR. M. R. CARO: I should like to disagree with the histologic diagnosis of lichen planus. The papillae were edematous; there was a loose cellular infiltrate that did not reach the epidermis, and there was no sharp line of demarcation at the lower border of the infiltrate. I thought a diagnosis of lichen striatus was more compatible with the condition in this case.

DR. E. A. OLIVER: This little girl presents a picture similar to that in 2 patients I have had under my care; one was a child and the other a man. In both the condition resembled linear lichen planus, and although no sections were taken, I did not believe it was that disease. Both patients responded readily to

treatment, the adult to fractional roentgen therapy and the child to ointments. I feel that the condition was lichen striatus.

DR. M. H. EBERT: If there must be a new dermatologic entity, I am pleased to have this type, one that disappears promptly with no treatment but with the dermatologist getting credit for doing good work. When I first saw this girl, three weeks ago, the arrangement of the lesions was striking, the lesions closely resembling those of lichen planus. The sudden onset impressed me. A section was taken, and when she came back the next time her skin was almost clear, with practically no treatment except a soothing lotion. I hesitated to present the case because she had no eruption as she did three weeks ago. I thought the microscopic picture was of lichen planus. There was hyperkeratosis and especially marked hypergranulosis. The edema of the rete was what one sees in acute lichen planus. The most striking feature was the fraying out of the lower cells into the infiltrate of the corium. As Dr. Caro says, the infiltrate is not as deep as in lichen planus, and the infiltrate in some places is about the blood vessels.

Dermatofibrosarcoma Protuberans. Presented by DR. DAVID V. OMENS and DR. WALTER W. TOBIN (by invitation).

T. S., a Negro aged 42, states that thirty years ago he fell off a bicycle and scraped his left hip, which on healing retained a silver dollar–sized scar. Eight years ago the scar thickened, and lumps began to form, which have increased in size and number. There are no subjective symptoms.

Examination discloses a palm-sized, freely movable area made up of scar tissue over the left trochanteric region, in which reddish and skin-colored nodules of varying size, some pedunculated, some sessile, are located. Telangiectatic vessels are present over some of the nodules.

The blood and the urine were normal. A histologic examination of a nodule showed thinning of the epidermis, numerous large bundles of connective tissue and spindle cells.

DISCUSSION

DR. FRANCIS E. SENEAR: I think this patient presents a classic example of the disease.

Pellagra and Myxedema. Presented by DR. THEODORE CORNBLEET and DR. DAVID COHEN (by invitation).

M. K., a Lithuanian woman aged 47, presents an eruption on the hands, forearms, elbows and thighs of six months' duration. At that time she began to have mental symptoms, such as hearing voices. The skin began to turn brown and thick. The patient was in Cook County Hospital in March 1939, where she remained until May, with the same symptoms and findings. At that time nicotinic acid, 100 mg. every four hours, was given, and she left the hospital free of symptoms.

She now presents a brownish scaling eruption on the dorsa of the hands, extending to the forearms and wrists and also over the elbows and on the inner side of the thighs. The areas are sharply demarcated. The basal metabolic rate is —47 per cent.

DISCUSSION

DR. M. J. REUTER, Milwaukee: I believe that the diagnosis of myxedema and pellagra is correct. I suggest that the extensive hyperkeratosis in the groin is probably a feature of myxedema rather than of pellagra. About eleven years ago, when working with Dr. O'Leary, I had an opportunity to see a number of patients with myxedema. It was not infrequent to find decided hyperkeratosis in the folds of the axilla and groin. Incidentally, myxedema clinically does not appear until the basal metabolic rate approaches —38 or —40 per cent.

DR. THEODORE CORNBLEET: I never saw this type of eruption in a number of pellagrins that I examined before coming to Chicago. At Cook County Hospital

I have been able to see several pellagrins who showed these well defined exudative and crusted lesions about the genitals and on the perineum. That picture was more evident last week than it is now. Treatment with nicotinic acid has caused great improvement.

Tuberculosis Verrucosa Cutis. Presented by DR. OLIVER S. ORMSBY and DR. WALTER W. TOBIN (by invitation).

M. B., a Negro aged 36, presents a verrucous, dirty grayish lesion on the left hand and a plaquelike scaly lesion made up of pea-sized nodules on the left shoulder and axilla.

The lesion on the hand began sixteen years ago, when the patient worked as a gutter in the Chicago stock yards. He states that while eviscerating an animal whose viscera were studded with small white lumps he accidentally scratched himself on the back of the left hand. Eighteen days later a sore developed in this area and enlarged. Three months later enlargement of the glands in the axilla developed, but the swelling went down, and shortly thereafter an eruption appeared on the shoulder.

The patient was seen first in 1936, at which time a test with a 1:1,000 dilution (0.1 cc.) of bovine tuberculin gave a positive reaction. A section taken in 1936 showed tremendous verrucous change, with an infiltrate of round and epithelioid cells.

DISCUSSION

DR. HENRY E. MICHELSON, Minneapolis: I think this case warrants discussion from many angles. First, to speculate on the course of events: This man was a gutter in an abbatoir. He received an injury, and a lesion developed. Evidently he had an external inoculation, and the question is, Did a primary complex develop or did he have tuberculosis before and did a secondary inoculation develop? The fact that suppurating glands developed suggests a primary complex. The fact that his condition lingered so long and was benign makes one think that possibly the first lesion was a verrucous form of tuberculosis or a primary complex. As time went on, the lesions evidently became more lupoid in character and evidently became classic lupus vulgaris. It is well known that in any type of inoculation tuberculosis transition to lupus vulgaris is common.

DR. RUBEN NOMLAND, Iowa City: I agree with Dr. Michelson and should like to state that four years ago the lesions in the axilla were flat. The biopsy specimen taken from the axilla early in the course showed typical tuberculous structure and showed no verrucous areas, while a biopsy of tissue from the hand showed little tuberculous change but much hypertrophy of the epidermis.

DR. PAUL A. O'LEARY, Rochester, Minn.: My concept of this disease differs from that of my colleague. I consider this condition as occupationally acquired tuberculosis. It would have been easy for the patient to become infected with the bovine tubercle bacilli, for a tuberculous primary lesion to develop, with its resulting adenitis, and to be followed, by the process of contiguity, by tuberculosis verrucosa cutis. Whether this man had a previously existing Ghon tubercle is, I believe, of less importance than the type of organism with which he was inoculated. Inoculation tuberculosis, with its characteristic inoculation chancre, pipestem lymphangitis and adenitis, may subsequently manifest various types of cutaneous tuberculosis in the region of the inoculation site. Tuberculosis verrucosa cutis, lupus vulgaris and scrofuloderma have been observed on my service. I have searched unsuccessfully for other systemic manifestations of tuberculosis in our patients, because the literature contains reports of patients in whom miliary tuberculosis and erythema induratum develop subsequently.

DR. OLIVER S. ORMSBY: I think Drs. Michelson and O'Leary have expressed the same opinion. They agree that the case is one of inoculation tuberculosis. As Dr. O'Leary stated, the infection occurred on the dorsum of the hand and extended by way of the lymphatics up the arm and invaded the axillary glands. Scrofuloderma then developed, with secondary involvement of the overlying skin

producing a verrucous type of tuberculosis. In most of the cases of verrucous lupus that I have seen, general dissemination of the organism of tuberculosis occurred after an attack of some condition such as measles, with the development of numerous verrucous lesions, particularly on the extremities. In the present case the disease has remained comparatively local and is not of hematogenous nature.

DR. J. H. MITCHELL: I think Dr. Nomland will recall an old man we had some years ago with an inoculation of the verrucous type on the right wrist. His infection occurred while he was weighing sputum in the Municipal Tuberculosis Sanitarium. He had a little injury and the inoculation followed. The bacillus was presumably the human type and remained at the site of inoculation.

DR. WALTER W. TOBIN (by invitation): I have seen this man once since 1936 (that was in 1938), and at that time he had a positive reaction from a tuberculin test with bovine tubercle bacilli. I do not remember whether a roentgenogram of the lungs was made at that time.

Hidradenitis Suppurativa. Presented by DR. MAX S. WIEN.

H. R. J., a white police officer, aged 42, was first seen in November 1939, bedridden because of extreme weakness and exhaustion subsequent to chronic discharging abscesses in both axillas, with greater involvement of the right axilla and associated involvement of the perineum and the perianal area of four years' duration. The drainage was so intense that it caused great discomfort and prevented the patient from working. During this time he also noticed increased loss of strength and vigor and had a low grade fever, with a temperature between 99 and 100.4 F. In November 1930 examination of the blood revealed anemia, with slight increase in the leukocytes.

A clinical examination of the heart and lungs showed no abnormalities.

He was first seen at Billings Hospital in May 1939, with draining sinuses in the axillas, anal region and groin. The Frei test for lymphogranuloma venereum gave a negative reaction. Inoculation of tissue into guinea pigs showed no tuberculosis. Pus from one of the lesions showed only diphtheroid organisms. The Kolmer and Kahn reactions of the blood serum were negative, and the urine showed 3 plus reduction with Benedict's solution. Fasting blood sugar was usually low normal, but a sugar tolerance test revealed an abnormal curve. The fasting sugar was 93 mg. at the beginning of the test, 208 mg. after one-half hour, 283 mg. at one hour, 175 mg. at two hours and 99 mg. per hundred cubic centimeters in three hours.

In view of the history and the results of laboratory tests, a diagnosis was made of hidradenitis axillaris which had extended to produce deep abscesses.

When first seen by me the patient presented the picture of cachexia and emaciation, with profuse thin purulent discharge from both axillas with greater involvement of the right. On extension of his right arm the axilla under tension revealed deep sulci, at the base of which were superficial ulcerations and pits that discharged pus. There was also thin purulent discharge in the perineal and scrotal area, with superficial ulceration and irregular margin to the border of the ulcers. On palpation of the margin of the right axilla, one could feel a definite boggy infiltrate that extended beyond the area of involvement and reminded one of the infiltration noted in erythema induratum (Bazin).

The right axilla is completely involved with red to reddish brown sulci with deep scarring approximating an irregular groove deep in the apex of the axilla. The entire area is moist with a thin seropurulent discharge that seems to well up from the depth of the irregular sulci produced by the scarring. There are also scarring and moderate discharge in the groin, of a less marked type, with cribriform scarring in the perineum and a linear band of irregular scarring radiating to the posterior aspect of the left thigh, which is dry and free of discharge. The patient's general condition is good, with considerable deposition of subcutaneous fat over the trunk and thighs, in contrast to the emaciation he presented when first seen.

DISCUSSION

DR. S. W. BECKER: I did not see the man today but I remember him. He was hospitalized at Albert Merritt Billings Hospital for some weeks, and the condition was studied by culture, microscopic examination and animal inoculation, and a tuberculous infection could not be demonstrated. It was considered hidradenitis of the type recently described by Brunsting (Brunsting, H. A.: Hidradenitis Suppurativa; Abscess of Apocrine Sweat Glands, ARCH. DERMAT. & SYPH. **39**: 108 [Jan.] 1939) at the Mayo Clinic. He had severe hidradenitis of the axilla and groin.

DR. PAUL A. O'LEARY, Rochester, Minn.: I agree with the diagnosis of hidradenitis suppurativa. In my early experience with cases of this condition I felt that surgical intervention was contraindicated, a belief based on the fact, as I now see it in retrospect, that surgical drainage of the infected area tended to spread and prolong the course of the disease. It is now the practice to operate on these patients after a few weeks of preparatory treatment directed toward reducing the infection as much as possible. Rather than merely incising the infected nodules, the entire involved area in both axillas or in the groin with the underlying glands is now surgically removed, and a full thickness skin graft is done at the time of the excision. The use of the skin graft has materially decreased the period of healing; now six to eight weeks is required for recovery, whereas formerly as many months or more was necessary.

Another point of interest is the relation of hidradenitis suppurativa to perifolliculitis abscedens et suffodiens. Both diseases are the result of infection of the apocrine glands, of which there are many in the scalp. The onset of hidradenitis suppurativa following infection in the hand or forearm, followed by extension to the opposite axilla, the groin or the anal cleft or occasionally under large pendulous breasts, emphasizes the fact that the disease is systemic rather than local.

DR. MAX S. WIEN: When I first encountered this case of hidradenitis I was impressed with the resemblance of the infiltrate to that in erythema induratum (Bazin). In a discussion by Pollitzer (ARCH. DERMAT. & SYPH. **41**:58 [Jan.] 1940) he stated that Philippson and he agreed on the essential features of certain remote cutaneous conditions and the group of tuberculids later described by Darier. The patient had a negative reaction to a von Pirquet test. He shows great improvement on a regimen of rest, fresh air and tonic therapy.

He was given roentgen therapy to the axillas, has gained 50 pounds (23 Kg.) since last September, is able to work again as a policeman, feels strong and is constantly gaining weight, as compared with his previous emaciated bedridden state.

HERBERT RATTNER, M.D., *President*

M. H. EBERT, M.D., *Secretary*

May 15, 1940

Erythema Figuratum Perstans. Presented by DR. DAVID V. OMENS and DR. WALTER W. TOBIN (by invitation).

B. K., a girl aged 11 years, states that two years ago a circular red patch appeared on the inner surface of each knee, the patch on the right knee still being present. About one year ago similar areas appeared on the thighs and on the back of the neck. They seem to fade at times but do not disappear. There is no itching.

The family and personal history are irrelevant.

Examination discloses palm-sized, annular and semicircular erythematous, scaling lesions on the nucha and the upper, inner aspects of the thighs and a circinate scaling patch above the right knee.

The urine and blood were normal. Histologic examination of one of the lesions on the thigh showed parakeratosis, moderate edema and an infiltrate of round cells mainly about the blood vessels.

DISCUSSION

DR. C. W. FINNERUD: I should like to ask how that diagnosis was arrived at. Neurodermatitis is sometimes seen which has much this appearance. I have seen neurodermatitis of the Vidal type in which circular segments were evident. I wonder if this condition could not be of that class.

DR. S. W. BECKER: I think this condition is a typical neurodermatitis of the Vidal type. The configuration is a little unusual, but a bizarre type is possible. I believe that this particular eruption lacks the rose red color and the central scaling of erythema figuratum perstans. The lesions are somewhat like lichenified plaques.

DR. M. E. OBERMAYER: I questioned the patient specifically as to the presence of pruritus, and she said that only mild itching was occasionally present. Though there is a certain clinical resemblance of the condition to lichen simplex chronicus, I feel that this diagnosis cannot be made in the absence of pruritus.

DR. MAURICE OPPENHEIM (by invitation): Lichenified areas are absent. It may be that the condition is some kind of erythema figuratum. I thought of another disorder, xanthoerythroderma pityriasiformis of Radcliffe Crocker, because it is so yellow and has an irregular configuration, not round and not annular, and because the skin shows a fine flower-like desquamation. I believe one must also think of a lesion belonging to the group of parapsoriasis. I did not see the histologic sections, which would decide the question.

A Case for Diagnosis (Hydroa Vacciniforme? Folliculitis Ulerythematosa Reticulata?). Presented by DR. THEODORE CORNBLEET.

Miss G. M., a white woman aged 19, has had a disease of the skin of the face, neck and upper extremities off and on for the past four years. The first episode began about Christmas time four years ago, lasted three or four weeks and subsided, with relief of all symptoms. The following winter the cutaneous trouble recurred about Christmas and remained for six weeks. The next episode was in August and September of 1939. Four weeks ago, following an appendectomy, the condition returned.

At present there is an eruption on the scalp, face, neck and upper extremities and about the ankles. On the upper extremities most of the lesions are on the extensor surfaces. The lesions consist of small pinhead-sized to pea-sized crusts and excoriations. There are pinhead-sized and slightly larger deep vesicles present as insets in a dry, chronic, diffusely inflamed skin. The backs of the hands suggest remotely the changes associated with mild pellagra. On the forehead especially there are follicular horny plugs. There is a fine reticulated pigmentation present mostly on the face and a fine atrophic scarring paralleling the pigmenting process, all having a meshlike pattern. The hyperpigmentation does not disappear between the episodes. There is moderate to severe itching only during the active periods. The general health is not affected, and the patient's diet has been and is adequate.

Laboratory Tests.—Urinalysis showed: deep amber color, 1 plus reaction for albumin, no sugar and 1 red blood cell per high power field. Examination of the blood showed: 85 per cent hemoglobin and 4,450,000 red cells and 13,100 leukocytes per cubic millimeter, with a differential count of 83 per cent polymorphonuclear leukocytes, 8 per cent lymphocytes and 9 per cent monocytes; the nonprotein nitrogen amounted to 28 mg. and the blood sugar to 107 mg. per hundred cubic centimeters.

The epidermis showed slight intracellular edema. In one place there was thickening of the epidermis and intercellular edema. Beneath this in the corium was a microscopic abscess containing many polymorphonuclear leukocytes, in addition to lymphocytes and histiocytes. There were mantles of the same type of inflammatory infiltration about the blood vessels and some of the hair follicles. The collagen fibers and elastic fibers were missing from the areas of infiltration but were intact elsewhere. Perles' prussian blue reaction was negative for iron.

DISCUSSION

DR. THEODORE CORNBLEET: I obtained a specimen of urine, but the quantity was insufficient to test chemically for porphyrin. Grossly the urine had a smoky appearance, somewhat in keeping with what one expects to find if much porphyrin is present.

NOTE.—The patient's urine was later examined for porphyrin; ten times the normal quantity was found in a twenty-four hour specimen.

DR. S. W. BECKER: This case is interesting, but it is difficult to make a definite diagnosis. The patient presents chiefly an excoriation, although she did have one bulla on the hand; this was a typical bulla and not the ordinary lesion seen in hydroa aestivale. The condition began when she was 16, which is the age at which acquired epidermolysis bullosa appears, though the face is an unusual location for these lesions. There is no history of the condition in other members of her family. It seemed to me she had linear crusts, as though there were excoriations rather than the type of lesion which would follow rupture of bullae.

DR. M. R. CARO: I thought that histologically there was hardly enough edema in the epidermis to fit in with the diagnosis of hydroa vacciniforme. The changes in the section were largely present in the corium and were of a type often seen in some varieties of pyogenic infection.

DR. OTTO H. FOERSTER, Milwaukee: The presence of distinct sensory abnormalities preceding the appearance of the eruption suggests that the condition is of the nature of hydroa vacciniforme and that photosensitivity may play a part in its production.

DR. THEODORE CORNBLEET: When I first saw this girl I looked carefully for the presence of vesicles or bullae, and none could be seen at that time. Several days later the patient was shown at the University of Illinois clinic, where several other staff members also did not find any vesicles. Several days after that there were definite vesicles present. Dr. Weber suggested the diagnosis of hydroa vacciniforme. Up to that time what impressed me a good deal was the reticulated atrophy present on the face and neck, together with a certain amount of pigmentation. I have an open mind about the final diagnosis in this case. It is noteworthy that a few days ago she was given an erythema dose of ultraviolet rays, and today erythema is present without any other changes.

A Case for Diagnosis (Parapsoriasis?). Presented by DR. M. H. EBERT and DR. A. H. SLEPYAN (by invitation).

The patient, a 72 year old scrap iron dealer, noted the onset of this eruption about five years ago. The lesions appeared progressively over the chest, the back, the lower part of the trunk and the sacral area, associated with only occasional itching.

Scattered over the entire back, on the extensor areas of the arms, in the axillas, over the sacrum and along the sides of the abdomen are discrete pinhead-sized to pea-sized areas of yellow brown atrophy, in places showing telangiectatic vessels. On the extensor surfaces of the arms are remnants of the scales that originally topped each lesion. The scales are yellowish brown, piled up and laminated and can be lifted off, leaving a smooth, glistening moist surface with occasional bleeding. On the scalp and face are numerous large comedos with considerable seborrhea. On the right leg the patient presents a large recurrent patch of stasis eczema of seven years' duration.

Examination of the blood showed 4,400,000 erythrocytes and 11,200 leukocytes per cubic millimeter, with a differential count of 52 per cent polymorphonuclear leukocytes, 12 per cent eosinophils, 8 per cent monocytes and 28 per cent lymphocytes. The Wassermann reaction of the blood was negative.

DR. OTTO H. FOERSTER, Milwaukee: My first impression of this unusual eruption was that it bore a close clinical resemblance to pityriasis lichenoides of subacute type. Further and more detailed examination led me to abandon that diagnosis and also that of leukaemia cutis, which was suggested to me more by

the microscopic picture, on hurried examination, than by the unusual eruption and other clinical features. The condition is new to me, and I have no diagnosis to offer.

DR. MAURICE OPPENHEIM (by invitation): This interesting case reminds me of cases described at first by Kyrle under the name hyperkeratosis follicularis in cutem penetrans, but the histologic picture excludes such a diagnosis. The most prominent symptom of the microscopic slides is a broad band of uniform round cells which infiltrate compactly the papillary and subpapillary layer, sharply limited from the reticular layer. In some places one finds a subepithelial blister formation. This reminds me in a certain degree of a lymphatic leukemic infiltration. There is no decided hyperkeratosis or acanthosis. It is impossible for me to make a certain diagnosis in this case.

DR. E. A. OLIVER: I am glad that Dr. Ebert demonstrated this case today. It has been under observation at St. Luke's clinic for some months. The eruption has differed somewhat from the eruption present now. It suggested psoriasis and parapsoriasis of the lichenoid type. The scaling was much more evident than it is now, and the smaller lesions bled when the scales were removed. I could not arrive at a diagnosis.

DR. C. W. FINNERUD: I am extremely puzzled but equally interested. My first clinical impression was that the condition was an unusual form of parapsoriasis. What impressed me most when I examined the histologic section was the possibility of the condition's being leukemia. I believe that the so-called Senear-Usher syndrome must also be considered, in that there are features of seborrhea, lupus erythematosus and, microscopically at least, vesicles.

DR. M. R. CARO: I think there are certain clinical and histologic features about this case that suggest the diagnosis of atrophic lichen planus. Dr. Zeisler and I presented a case some years ago (Zeisler, E. P., and Caro, M. R.: Lichen Planus with Fatty Infiltration, ARCH. DERMAT. & SYPH. **29**:130 [Jan.] 1934) that was similar in many respects. In that case there were, in addition, some silvery streaks on the buccal mucosa and on the palate. The presence of keratotic follicular plugs in the skin can also be considered as being part of the picture of lichen planus, for such plugs were present in another case presented before this society (Caro, M. R.: Lichen Planus, ibid. **28**:725 [Nov.] 1933). The histologic picture in this case, while not pathognomonic, is also consistent with the diagnosis of atrophic lichen planus.

DR. MINNIE PERLSTEIN: I have seen this patient on numerous occasions since 1928. The last time I examined him was two years ago, at which time he presented no evidence of the eruption seen today. Since 1928 he has been hospitalized on two or three occasions because of chronic eczema on the legs and at times because of acute seborrheic dermatitis involving his chest and back. I at no time performed a biopsy, but the clinical picture seen today is entirely different from that shown at any previous time.

DR. M. H. EBERT: I am grateful for the discussion and for the various suggestions in the way of diagnoses. This case is unique; I have never seen a condition like it. I found it difficult to coordinate the clinical and histologic observations. When the patient was first seen the picture was considerably different from what it is now. The lesions that were described on his back were covered with crusts and presented a greasy appearance. The follicular lesions on the scalp and chest were about the same as today. My first diagnosis was Darier's disease. After picking off the scales I was not so certain. I was certain I had never seen a condition like it before. On looking at the histologic section this morning it occurred to me that there might be a possibility of lymphocytoma described by Epstein. Dr. Nomland had 2 or 3 cases of this at the Central Free Dispensary, benign tumors consisting of accumulations of lymphocytes and proliferation in situ. The lymphocytes were evidently preformed in that area. I also had a case of this kind which did not resemble this. It would be hard to fit that diagnosis in with the lesions in the peripheral vessels, the erythematous macules on the soft palate and the keratotic plugging of the hair follicles on the scalp.

I also considered Spiegler-Fendt sarcoma, but I have never heard of a tumor of that type breaking down and healing with this type of scar. I cannot throw any more light on the subject but simply speak of the various speculations. I think Dr. Finnerud's theory is a good one to follow. It would be worth while to consider lichen planus and seborrheic dermatitis, suggested by Dr. Caro. I do not know what more work can be done.

Acrodermatitis Chronica Atrophicans. Presented by DR. M. H. EBERT.

A. K., a married Ukranian woman aged 42, complains of changes in the skin of the lower extremities of one and one-half years' duration. This condition started as a red patch on the right knee, spread to the remainder of the extremity and is associated with itching. The left extremity was involved two months later after an injury to the left knee.

The past history reveals that an operation was performed on the left side of the neck during infancy for an unknown condition. Five years ago a pelvic operation was performed following a miscarriage associated with severe metrorrhagia. She has three children living and well.

The process involves the lower extremities and extends on the buttocks and over the sacrum. The involved area is bluish red with atrophy. The superficial veins are prominent in all areas. The feet are cold and cyanotic, and there is considerable infiltration over the dorsa. The thighs present small shiny atrophic white areas alternating with violaceous-red areas, causing a mottled appearance. The skin over the right knee is infiltrated and arranged in transverse folds. Over the left patella at the site of a bruise which occurred in January 1940 there is a dark brown linear infiltrate covered with a silvery scale.

DISCUSSION

DR. S. ROTHMAN (by invitation): The history of this patient reveals early menopause, which is often found in patients with acrodermatitis chronica atrophicans. Although this fact has been mentioned in the literature several times its possible importance as regards the pathogenesis has not yet been investigated.

This disease seems to be rare in this country as compared with its incidence in central European states, where it is a rather common cutaneous disease.

DR. E. P. ZEISLER: I think it is worth while commenting on the scleroderma-like condition around the ankles and below the knees.

DR. MAURICE OPPENHEIM (by invitation): This eruption is typical of acrodermatitis atrophicans. There are two clinical features present which determine the final stage of this disease: first, the lipomatosis, which is distinct above the patellar region, where there are two pillow-like soft tumors which are due to the fact that the subcutaneous fatty tissue is growing after the degeneration of the tissue in the cutis (substitution *en vacuo*); second, the so-called pseudoscleroderma tous changes of the skin on both legs, to which Dr. Ebert directed attention. A third final stage is acrofibromatosis, distinguished by the formation of fibromas at the extensor surfaces of the joints, this condition being absent in this case. The increase in connective tissue is caused by the degeneration of the elastic fibers, which inhibit the overgrowing of the connective tissue fibers.

An interesting fact is that so few cases of dermatitis atrophicans are observed in this country. Many cases have been observed in Vienna, and many more were published by Pautrier in Strasbourg.

DR. M. H. EBERT: I was pleased to hear Dr. Oppenheim's comments because I know he has done a great deal of work on this subject, particularly on the various changes that are associated with acrodermatitis, like new formations of elastic tissue and lipoidosis.

Argyria. Presented by DR. M. H. EBERT and DR. D. V. OMENS.

G. S., a 44 year old Polish man, has noticed a discoloration of the skin for the past six years. Fifteen years ago he underwent the first of six mastoid operations in five years, after which he used a 20 per cent solution of mild protein

silver as nose drops three or four times a day for nine years before he noticed a grayish discoloration of the skin of the face and neck. After that he continued using the solution only when the throat became dry, perhaps once a day or so up to the present time. Otherwise the patient has considered himself in good health.

Examination of the skin discloses a diffuse dark slate gray discoloration of the entire face, including the conjunctivas and the mucous membranes of the mouth. The color becomes gradually lighter on the neck, trunk, extremities and parts which have been covered by clothing. The nail beds are also slate gray.

DISCUSSION

DR. A. W. STILLIANS: I thought this case was interesting. The brown color, instead of the blue usually seen, I thought might be due to the fact that the skin is the type in which melanin develops easily.

DR. THEODORE CORNBLEET: One of my patients with argyria was studied by the hematologists. She showed evidence of a partial blockage of the reticulo-endothelial system. On looking over the literature I did not see any work done to corroborate this observation. It would be interesting to observe other patients with argyria to see if they, too, show such blockage.

Localized Solid Edema of the Extremities (Myxedema). Presented by DR. FREDERICK R. SCHMIDT.

C. K., a woman aged 43, is presented from the outpatient department of Grant Hospital. She entered the dermatologic clinic two weeks ago, complaining of pain in the legs with unsightly swelling. She had noticed swelling of the legs a year ago, but it had been intermittent. At that time she was nervous and was losing weight. The basal metabolic rate was +35 per cent. Thyroidectomy was performed in January 1940. A month ago the swelling of the legs became more noticeable. The basal metabolic rate on May 8 was —20 per cent.

The systolic blood pressure is 120 and the diastolic pressure 76. The cholesterol content of the blood is 220 mg. per hundred cubic centimeters.

On the anterior surface of both tibias, from the external malleoli a third of the way up the legs, are two well defined tawny, nonpitting, slightly reddened, elevated plaques. The skin is like pig skin in these areas. It is dry, waxy, translucent and firm. There is no evidence of inflammatory reaction.

DISCUSSION

DR. L. M. WIEDER, Milwaukee: I think this clinical picture is usually thought of as being associated chiefly with hypothyroidism. The cutaneous changes were noted by the patient while he had a highly elevated basal metabolic rate. It is interesting that the condition became intensified after the thyroidectomy, and since then the basal metabolic rate has been lowered to —20 per cent.

DR. FREDERICK R. SCHMIDT: In looking over the literature I ran across articles by Arzt (Arzt, L.: *Med. Klin.* **30**:49 [Jan. 12] 1934) and O'Leary (O'Leary, P. A.: ARCH. DERMAT & SYPH. **21**:57 [Jan.] 1930). Dr. O'Leary published a series of 8 cases. A peculiar fact is that this particular type of circumscribed edema of the legs appears almost exclusively in patients with a metabolic rate above normal, in other words, in persons with hyperthyroidism. The other forms of myxedema—whether this case is one of true myxedema or not is not known—occur in persons with hypothyroidism.

A Case for Diagnosis (Infectious Granuloma?). Presented by DR. M. H. EBERT.

C. T., a 59 year old married Negress, had multiple eruptions on her buttocks five years ago which she treated with heat and various ointments. In 1937 she had "big boils" in the same region and was treated surgically at a hospital, after

which she was symptom free for two years. In July 1939 she noticed some "bumps" developing about the anus, which have grown larger and are accompanied by a discharge necessitating the wearing of a pad. She has had no change in bowel habits and has only occasionally taken laxatives. The bowel movements have been well formed, soft and of the same size. She estimates that she has lost about 20 pounds (9 Kg.) in the past three months. There was no history of cancer in the family. Her husband had tuberculosis and at present is living and well.

Physical examination showed no abnormalities except signs of some emaciation. About the anus on both inner surfaces of the buttocks is a fungating granulomatous growth that bleeds easily. The one on the left side is about the size of a grapefruit, measuring 12 by 6 by 5 cm., with indurated base and multiple sinuses, while the mass on the right buttock is about the size of an apple, measuring 3 by 10 by 4 cm. On the left buttock a sharply circumscribed coin-sized lesion is present lateral to the granuloma.

A specimen for biopsy taken from the top of the granuloma by the intern in the surgical ward to which the patient was admitted was reported as a mucus-producing adenocarcinoma, probably metastatic, from the rectum.

A Frei test gave a negative reaction. Smears for Donovan bodies have been negative.

A specimen for biopsy taken from the base of the granuloma and examined by Dr. Caro fails to confirm the diagnosis of adenocarcinoma, and the histologic picture looks like that of an infectious granuloma.

DISCUSSION

DR. M. R. CARO: In the slide I examined I could find no evidence of carcinoma. The histologic picture was that of an infectious type of granuloma.

DR. M. H. EBERT: The clinical diagnosis in this case was granuloma inguinale from the first. Several attempts were made to find Donovan bodies, but they were unsuccessful. I still feel that that is the diagnosis. Some of the material was sent to the department of surgical pathology, and a report of adenocarcinoma was made, which led to the taking of another specimen for biopsy. There was no evidence of carcinoma. I think the condition is granuloma inguinale.

DR. MINNIE PERLSTEIN: In the course of a study of lymphogranuloma venereum, I performed many biopsies on various manifestations of this condition. Not infrequently, on examination of tissue from an ulcerated lesion, the report from the laboratory would be that the condition was a carcinomatous lesion. This observation is entirely in accord with Dr. Weidman's report of carcinoma-like changes occurring in a chronic ulcerative process.

Toxic Eruption Following Injections of Sodium Morrhuate. Presented by DR. M. R. CARO and DR. L. F. WEBER.

Miss M. B., aged 18, noticed an eruption seven days ago on the upper and lower extremities, face and trunk. She received five injections of sodium morrhuate for the obliteration of varicose veins of the legs. On April 26 she received two more injections of sodium morrhuate. One day later tenderness appeared at the site of injection and in the surrounding area. The right leg, the site of the injection, showed redness and edema. On May 8 the generalized eruption appeared; it is erythematous and papular. The condition is more severe on the upper and lower extremities. Subjective symptoms consist of burning and itching.

DISCUSSION

DR. S. W. BECKER: I have seen cutaneous eruptions follow the use of sodium morrhuate for obliteration of veins, but they were all allergic, never of this type.

DR. L. F. WEBER: Our experience has been limited to 2 patients. We have checked the records in the surgical department, and according to them the patients

have not had many reactions of any type. I know reports have been made of asthmatic attacks and urticarial attacks following injections of sodium morrhuate. In both of our patients the causes have been similar. There was a severe reaction at the site of injection, and within a day or two a generalized toxic eruption appeared. In the other case the condition ran its course in twelve days. This patient has made some improvement in the last two days. I think in another few days the eruption will be practically cleared up. I have searched the literature for reports of toxic eruptions following sodium morrhuate but so far have not found any. I was also questioned about what substance or what part of the sodium morrhuate was the damaging agent. I am unable to answer that. So far I am still of the opinion that the reaction in the leg was a thrombophlebitis. It is important to know the causation of the toxic eruption.

DR. M. E. OBERMAYER: To make certain that the condition is a toxic eruption from sodium morrhuate it might be worth while to continue the injections with monolthanolamine oleate instead. The latter supposedly contains no protein, and if injections with that compound are unaccompanied by toxic symptoms it would seem fair evidence that the proteins contained in sodium morrhuate were responsible for the eruption. However, in my experience, even monolate may occasionally cause toxic eruptions, though of a milder degree.

DR. L. F. WEBER: I have felt that this toxic reaction has not pursued the course of a protein reaction. Both of the patients have had five or six injections. I thought that was not the usual course of a protein reaction.

DR. FREDERICK R. SCHMIDT: A condition similar to this occurred at Grant Hospital. The curious thing is that the eruption was not limited to the legs but involved the face and neck, with little on the trunk. I wonder if there is a factor of sunlight present, for the lesions in that case were limited to the exposed skin.

DR. L. F. WEBER: The condition was more noticeable on the face two days ago than today.

Adenoma Sebaceum and Tuberous Sclerosis. Presented by DR. MINNIE PERLSTEIN.

J. V., a boy aged 12½ years, presents the following history. He was apparently developing normally until he was 18 months of age, when he had a convulsion associated with a right hemiplegia. After this he seemed duller than before and did not begin to speak until he was 3 years of age. He had a second convulsion at 6 years of age and since then has had attacks about every six to eight weeks. His mental condition has been slowly regressing.

On examination, he appears dull but cooperative. Scattered over the flush areas of the face are discrete, isolated and grouped pinpoint-sized to match head–sized bright red, firm papules. There are small depigmented areas scattered over the body, with numerous subcutaneous fibrous nodules located especially over the sacral area. The physical examination otherwise gave essentially negative results except that on ophthalmologic examination definite sclerosis of the fundus of the right eye was observed. His intelligence quotient was 67, with marked scatter.

Encephalography, by Dr. Meyer Perlstein, showed normal cortical markings, dilated lateral ventricles, especially on the left side, deviation of the septum pellucidum to the right and a calcified area at the base of the left lateral ventricle in the choroid plexus. The encephalographic diagnosis was left internal hydrocephalus; a calcified or sclerotic patch was observed in the left choroid plexus, approximately 1 inch (2.5 cm.) above the sella turcica and to the left of the midline. The sella was unchanged. Electroencephalography showed abnormal waves in the left motor area.

In summary, this 12 year old boy presents the syndrome epiloia, which includes epilepsy, due to sclerosis of the choroid plexus in the left lateral ventricle, adenoma sebaceum, associated with vitiligo and neurofibromas, and mental deterioration.

DISCUSSION

DR. OTTO H. FOERSTER, Milwaukee: The association of tuberous sclerosis and epilepsy has been known for many years. About thirty years ago, in company with a neurologist, Dr. N. S. Yawger of Philadelphia, I examined a large number of inmates of an epileptic colony and found that some of them had more or less well developed adenoma sebaceum. A number of these patients died some years later, and I was informed by the neurologist that autopsies on several with adenoma sebaceum had disclosed the presence of tuberous sclerosis.

DR. MINNIE PERLSTEIN: This boy presents the typical picture of epiloia; namely epilepsy, mental deterioration and eruptions of the adenoma sebaceum type. His mental age is roughly about 6½ years, and he is in the sixth grade of a school for mentally deficient children. His mentality is gradually decreasing, a fact of which he is aware. There is no history of any familial tendency in this direction. The other three children in the family are apparently normal. In addition to the sclerotic patches seen over the sacral area and those seen on encephalographic examination, there is also evidence of a sclerotic patch in the retina.

NEW YORK DERMATOLOGICAL SOCIETY

FRANK C. COMBES, M.D., *President*

J. GARDNER HOPKINS, M.D., *Secretary*

April 23, 1940

A Case for Diagnosis (Circumscribed Scleroderma of the Cheek?). Presented by DR. FRED WISE.

Dr. A., a physician aged 32, is in good general health. The past personal history is irrelevant. About six weeks ago he noted an area of baldness on the bearded region of the right cheek. This area is oval, about 2 inches (5 cm.) long and 1½ inches (4 cm.) broad, with fairly well defined borders. The condition resembles alopecia areata, but palpation discloses that the involved portion of the cheek not only is devoid of hair but is indurated to a slight degree. The patient states that the loss of hair preceded the onset of the induration. Subjective symptoms are absent. About nine months ago the patient had extensive dental work done on both sides of the mouth, requiring from six to eight roentgenograms. There are no signs of dermatitis, dryness of the skin or other evidences of excessive exposure to roentgen rays on either cheek, nor has the patient noted a previously existing inflammation of the skin of the face. No treatment has as yet been prescribed.

DISCUSSION

DR. HOWARD FOX: It is difficult to make a diagnosis in this case. The patient presents an obvious patch of alopecia areata, which on manipulation apparently shows an urticarial reaction. It does not have the color, consistency or lilac border of morphea.

DR. EUGENE F. TRAUB: I agree essentially with what Dr. Fox said. There is certainly no glazing of the skin. The skin does not look generally infiltrated over the whole area, nor does it look thinned or atrophic.

DR. A. BENSON CANNON: I think the case is one of amyloid degeneration or, possibly, of superficial sarcoid. The lateral and lower parts of the lesion are infiltrated and raised, and one can make out the lobulated structure in the infiltrated portion, somewhat resembling the shape of a four leaf clover. I think that a biopsy will be necessary in order to establish a diagnosis.

DR. R. H. RULISON: I am wondering whether this condition may not be just alopecia areata which perhaps has been self treated, resulting in some inflammatory reaction.

DR. FRED WISE: The fact that the alopecia preceded the infiltration is a puzzling feature of the condition.

A Case for Diagnosis (Capillary Nevus?). Presented by DR. J. GARDNER HOPKINS.

F. Z., a girl aged 3½ months, presented no abnormality at birth. When she was 2 months old a dark red area suggesting hemorrhage was noted. The left cubital fold and the left hand were deeply cyanotic and became normal in color when the arm was held extended. She was seen again at the age of 3 months. The red area at the elbow was more evident, and both lower extremities became cyanotic when she cried. Ten days later an irregular dusky appearance was noted on the upper anterior portion of the left side of the chest, in the left axilla and on the outer surface of the left arm. The color in all of these areas disappears on pressure, and the dilated vessels fill slowly when pressure is released. Otherwise there seems to be little that is unusual about the lesion.

DISCUSSION

DR. EUGENE F. TRAUB: This condition is probably a naevus flammeus, just beginning. I should leave it alone.

DR. A. BENSON CANNON: I also think that the condition is a naevus flammeus and not sufficiently pronounced to warrant treatment of any sort, but I believe that blistering doses of ultraviolet radiation would be my choice of treatment should the parents want the blemish removed.

DR. HOWARD FOX: I agree with the diagnosis but consider it unusual for a naevus flammeus to make its appearance as late as two months after birth. As the treatment of naevus flammeus is always difficult and usually unsatisfactory, I advise that none be given in this case.

DR. FRED WISE: I also agree with the diagnosis, and I should be especially concerned about possible involvement of deeper structures.

Extensive Lupus Vulgaris Treated by Surgical Methods. Presented by DR. EUGENE F. TRAUB.

H. M., a woman aged 46, suffered from extensive lupus vulgaris which involved the greater portion of the scalp, scattered areas on the lower part of the abdomen, the labia and the perineal area, extending posteriorly to the buttocks and about the rectum. In addition to the cutaneous lesions, the patient has pulmonary tuberculosis, as demonstrated by roentgenograms. She does not have a cough or other clinical evidence of this disease, however.

The patient has received a great deal of treatment, without any success. In 1938 extensive surgical excisions with plastic repair were made by Dr. Herbert Willy Meyer. The results have been excellent, and there have been no recurrences of the condition.

DISCUSSION

DR. HERBERT WILLY MEYER (by invitation): This case is interesting from several points of view. One is, as Dr. Traub stated, that he did not believe dermatologic treatment would be of any further avail. The patient had been at the Leahy Clinic in Boston and at several other institutions.

I first excised an area on the forearm and performed a Thiersch graft, taking the skin from the thigh. Microscopic examination of the tissue removed showed typical lupus vulgaris. Having had good results with this, I next excised an extensive area on the forehead and performed a Thiersch graft. When that wound had healed, a few weeks later, I excised all of the remainder of the scalp which was involved over the bony part of the skull, and another Thiersch graft was done. A few weeks later I excised the rest of the area on the back of the neck and grafted that also. The grafts healed well.

The patient had an extensive area on the buttocks and was unable to sit because of painful ulcerations over the sacrum. I therefore excised this area right down

to the fascia over the muscles and up to the mucous membrane of the anus. In order to give her some soft tissue on which to sit, I made parallel incisions to the excised wound and undermined the skin of the buttocks on each side, sliding these flaps over to the midline of the exposed area and leaving defects on either side, which were covered with skin grafts. I sutured the mucous membrane of the anal margin to the flaps. There was a little difficulty in healing because of a collection of fluid, but healing did take place, and she is now able to sit in comfort. In fact, she has just returned from a motor trip to California.

The patient also had a rather large area on the lower part of the abdomen, down to the labia majora on either side of the vagina. I excised this area, including the labia majora, sutured the latter and repaired the defect with skin grafts. All of this work was not done at the same time. It was done in stages. I took two crops of skin grafts from the thigh. For the work on the lower part of the abdomen I took the skin grafts from the same thigh. There was also an extensive lesion on the ear. I excised the skin of the ear down to the cartilage and performed another Thiersch graft. These grafts were split skin grafts. This work was done in 1938. There were four separate operations. The patient was in the hospital from March to May 1939 and again from October to January. There has been no recurrence in the scars. There is one small new spot present now on the abdomen but not in the scarred areas.

DR. HOWARD FOX: The result is excellent, as two years has elapsed without any sign of recurrence. I have long considered that surgical excision was perhaps the best method of treating small patches of lupus vulgaris. In this case the surgeon is to be congratulated for his courage and skill in operating on such extensive and numerous areas. The results are most encouraging, in view of the shameful neglect or, at best, the poor treatment of lupus vulgaris in this country. I know of no Finsen institute in the United States similar to the many that exist in Europe. The reason is perhaps the comparatively small incidence of the disease in this country. One feature of lupus vulgaris which makes a radical cure difficult is the frequent involvement of the mucous membranes. That was fortunately absent in this case. As lupus vulgaris does not often occur coincidentally with pulmonary tuberculosis, I should like to ask Dr. Traub whether the roentgenogram of the chest indicated active tuberculosis in the opinion of the roentgenologist.

DR. HERBERT WILLY MEYER: Dr. Thorburn saw this woman in consultation. She has no cough and raises no sputum. Her temperature has not been elevated. She has no clinical signs of a pulmonary lesion, although the lesion is evident on the roentgenogram. All of the pathologic specimens were examined at the Lenox Hill Hospital, and all showed typical lupus vulgaris.

DR. J. GARDNER HOPKINS: Heretofore in undertaking operative removal of areas of lupus, there has been fear of infection in the scar. It is extremely interesting that the surgeon was able to do such extensive removal without the patient's incurring any infection.

DR. PAUL E. BECHET: I presented a patient before the Manhattan Dermatologic Society this month (ARCH. DERMAT. & SYPH., to be published) with extensive tuberculosis cutis of one buttock. The disease had been present for approximately fifteen years. A large section of the lesion had been excised at Mount Sinai Hospital six years previously, and there has been no recurrence in the excised area. The scar is smooth and not at all unsightly. The diseased areas not excised have extended until a considerable part of the buttock is involved.

Lupus vulgaris in certain instances can be just as mutilating and as malignant as carcinoma, and it should be treated just as vigorously. I have observed several cases in which the disease was extensive and spread to two and three times its former size after five or eight years of local cauterization with mild escharotics, roentgenotherapy, salt-free diets and timid electrodesiccation. The excellent results of surgical excision and skin grafting as demonstrated in Dr. Traub's case bring

to my mind the fact that this method of treatment offers in certain instances—depending on the severity, location and degree of the condition—such apparent permanence of cure as to warrant its more frequent use.

DR. EUGENE F. TRAUB: It is not known how rapidly the pulmonary tuberculosis is spreading, because the patient has no clinical symptoms. An active process seems to be going on, however, because since the first roentgenogram was taken two years ago there has been definite advancement in the condition, according to the roentgenogram taken a few days ago. I presented this case because I have several times heard it said that surgical therapy is not particularly good in cases like this because of the possibility of recurrence in the scars. I know this method has been practiced at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, and I have followed many of the cases for twenty years; I remember only 1 or 2 in which there were recurrences, provided the excision was properly done. In a number of cases ears have been involved, and new ears have been constructed. I have several patients now being treated for new spots on the body, but the newly constructed ears are doing well, with no local recurrence. One of the most interesting points to me was to find out whether lupus vulgaris might not develop in the area from which the grafts were taken. The area on this patient's thigh which had been used over and over again was smooth and showed no signs of tuberculosis. I think Dr. Meyer is particularly to be congratulated for the way in which he handled the area around the anus and buttocks. One would ordinarily expect lupus vulgaris to be dry and nonulcerative, with the skin unbroken. However, she had a large number of abscesses on the buttocks where the skin had broken down. I treated her with a great many bland remedies for a while, thinking that the ulcerated area was so extensive it might heal and cure itself. However, that did not occur. Dr. Meyer had, therefore, not only to excise a tremendous area of lupus vulgaris but to go deep to excise the abscesses. The idea of moving the skin from the lateral side of the buttocks over to the midline to cover the bad area and graft the sides thus left exposed was a brilliant one. It was done so that she would be able to sit comfortably and defecate without danger of contamination of newly grafted skin.

Pruritus (Icterus); Carcinoma of the Gallbladder. Presented by DR. A. BENSON CANNON.

E. L., a widow aged 64, consulted me on April 10, 1940, complaining of severe generalized itching with the formation of nodules. Her family history is not significant. Her husband died at the age of 55, of an unknown cause. She has a daughter, aged 40, who is partially paralyzed. She has had no miscarriages. At the age of 48, sixteen years ago, the patient was treated surgically for fibroid tumors of the uterus. The onset of her present condition occurred six months ago, with severe generalized itching which was most pronounced over the lower extremities. Itching caused loss of sleep and nervousness. Her physician gave her injections of a calcium compound intravenously and local remedies for relief of the itching, as well as some "pink tablets" to help her sleep. She has lost about 20 pounds (9 Kg.) in weight in the past four to five months and tires more easily than usual. In the last two or three months she has noticed many red nodules on the skin, especially on that of the extremities. Small, red, intensely itching papules appear in the skin. She has had no other treatment.

Examination shows a thin, pale woman who appears much younger than she is. Her complexion is sallow and slightly yellowish. The scleras are white with a yellowish tinge; the mucous membranes are pale, and the tongue is smooth, shiny and yellowish red. The skin of the body and extremities is yellowish brown and muddy, giving a mottled appearance with darker and lighter areas. There are many superficial excoriations especially evident on the extremities, with pea-sized whitish scars surrounded by a pigmented margin. Some of the recent scars have infiltrated edges. There is an occasional brownish red, split pea–sized, conical papule surrounded by a firm, hard infiltration that is felt but not visible. All the superficial glands are palpable, the size of a small pea, firm and freely movable.

There has been a pronounced loss of hair in the last four to five weeks, with almost total alopecia in back and around the sides of the scalp. Both the liver and the spleen are palpable. The liver is not much enlarged. In the right upper quadrant of the abdomen is a noticeable bulging. Just to the right of and above the umbilicus is a sharply demarcated, hard, irregularly shaped mass that is movable but is apparently attached to some deeper organ, being situated over the region of the gallbladder or the head of the pancreas. The mass is the size of an orange. Percussion over this mass gives a note of flatness. The heart is not enlarged. A short systolic murmur is heard over the precordium and is loudest over the aortic area. The blood pressure is 142 systolic and 78 diastolic.

Roentgenograms of the lungs, the mediastinum and the gastrointestinal tract were all normal. A large mass was seen, apparently attached to the head of the pancreas, with involvement of the gallbladder. The liver was also enlarged. The roentgenologic diagnosis was probable primary carcinoma of the pancreas. The Wassermann, Kahn and Hinton tests gave negative results. The results of chemical examination of the blood were normal. The icteric index was 18. Urinalysis showed a trace of albumin and 25 to 50 white blood cells, while the test for the bile gave positive results. A blood count showed 2,650,000 erythrocytes per cubic millimeter, with 40 per cent hemoglobin and 11,500 leukocytes per cubic millimeter, with 70 per cent polymorphonuclear leukocytes, 22 per cent lymphocytes, 6 per cent monocytes and 2 per cent eosinophils.

DISCUSSION

DR. R. H. RULISON: I agree with the diagnosis. I think the patient has a malignant growth in the abdomen, with secondary cutaneous changes.

DR. HOWARD FOX: I agree that the patient probably has a visceral carcinoma, but I did not see any clinical evidence of jaundice. The scleras were apparently normal, as I compared their color with that of the scleras of some of the members of the society. There was a generalized pigmentation, which I thought was probably due to the malignant condition. The increase of bile in the blood, however, might well have accounted for the itching.

DR. EUGENE F. TRAUB: I thought this patient had clinical jaundice. While it is not very evident in the scleras perhaps, even the mucous membranes of the mouth showed it well, particularly the tongue. I think the carcinoma is most likely in the head of the pancreas and not in the gallbladder. That is the usual location with this type of syndrome.

DR. J. GARDNER HOPKINS: The patient appears to be jaundiced and probably has been for a long time, but the jaundice is rather mild. Would mild jaundice of long duration account for the pruritus? I suspect it would. Or could the pruritus be perhaps accounted for by the atrophic changes in the skin?

DR. PAUL E. BECHET: The patient may have an icteroid pruritus, but there is not much corroborative evidence of it. She presents no definite symptoms of jaundice. The lesions are most noticeable on the lower part of the legs, where they present scooped out excoriations and not scratch marks. I would class the eruption as neurotic excoriations in a woman who has a carcinoma rather than as generalized pruritus due to icterus.

DR. FRANK C. COMBES: I agree that the patient has some jaundice and probably has some pruritus. Patients with pruritus due to jaundice do not usually scratch as this woman does. There may be some neurotic factor present. She has dug out punctate areas. Patients with jaundice tend to scratch with the palm, as do persons with urticaria, rather than with the nails.

DR. A. BENSON CANNON: The inference that the abdominal tumor is responsible for all the symptoms cannot be evaded. The itching was the primary symptom, followed by the appearance of urticarial papules, excoriation, scarring and pigmentation and infiltration around the scars. It is not remarkable to encounter patients with severe jaundice but no itching and still others with no clinical evidence of jaundice (only a high icteric index) but with intense pruritus.

A Case for Diagnosis (Leukemid?). Presented by Dr. Eugene F. Traub.

H. G., a woman aged 49, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, complains of an eruption which began a little over three months ago on the arms, neck and face and suggests an early stage of dermatitis of the contact type. It was thought that possibly the eruption was due to dye in one of her dresses, a woolen sweater or some other material contacted by her. The eruption on the face and neck cleared up, but the eruption on the arms has continued; it has itched intensely, and the skin is now thickened and lichenified. In addition, in the past three or four weeks, an entirely new type of papular eruption has developed, confined largely to the thighs and both legs. These papules have a definite infiltrated feel, are a little darker yellowish brown than the normal color of the skin and are discrete, with no tendency to confluence. They do not suggest a lichen planus papule in their size, location in the skin or color. There is no scaling.

Histologic examination of a papule showed the following features: In the center of the section was a small area in which the epidermis was acanthotic and platelike. The lower border was edematous, and in part the basal cell margin was absent. The granular and horny layers were present. In the upper part of the cutis there was a moderate bandlike cellular infiltrate extending up to the epidermis and composed chiefly of small round cells. Incidentally, beneath the lesion was a neurofibroma which was composed of bundles of fibrous tissue throughout which there was a diffuse infiltrate of fibroblasts.

Examination of the urine for arsenic and lead gave negative results. A complete blood count showed a severe secondary anemia, as manifested by anisocytosis and a moderate degree of poikilocytosis, with considerable achromia and some polychromatophilia.

DISCUSSION

Dr. Fred Wise: I do not think that the eruption is one of lichen planus. The eruption resembles leukemid, although I would not have thought of that condition unless I had some additional evidence to bring it to my mind. As to the lesions on the arms, I believe that the constitutional disturbance, whatever it is, caused the scaling and hyperpigmentation. They are probably two different manifestations of the same disease.

Dr. A. Benson Cannon: I agree with Dr. Wise that this condition is probably leukemid, although I am not at all positive. I believe that the patient should have a more thorough investigation before a definite opinion of the eruption is given.

Dr. R. H. Rulison: I agree with Dr. Wise that the trouble has some primary lesion which is probably internal, and I think the dissimilar cutaneous lesions are probably from the same source. However, what that is I do not know.

Dr. J. Frank Fraser: I agree with the views expressed by Dr. Wise but should like to add that in my opinion the histologic picture harmonizes more with the clinical diagnosis of leukemid than with that of lichen planus.

Dr. Eugene F. Traub: When this patient first came in I thought she had a most peculiar discoloration of the skin of the face and of the body generally. The skin has a peculiar cast, so much so that I thought of a possible icterus, but that was excluded. Then the question arose of secondary or pernicious anemia. The blood count, of course, is that of a peculiar type of secondary anemia. I think that there is some type of peculiar constitutional disease from which she is suffering and that the cutaneous lesions are secondary to that. I could think only of leukemia, but I have nothing to substantiate that diagnosis. I sent that diagnosis with the specimens to Dr. Satenstein. He did not comment on it but made a diagnosis of early lichen planus, which I do not think this case suggests clinically. Dr. Fraser, I believe, stated the opinion that the histologic picture is not inconsistent with a diagnosis of leukaemia cutis or leukemid.

A Case for Diagnosis (Mycosis Fungoides? Leukemid? Hodgkin's Disease of the Skin?). Presented by DR. FRED WISE.

M. F., a pharmacist aged 28, born in England, a patient of Dr. Jack Wolf, was first examined on July 12, 1934, complaining of an eruption of three years' duration, which began as a hard red plaque the size of a nickel on the anterior part of the chest. Another similar lesion appeared on the midportion of the back, and then tumors gradually appeared on other parts of the back, on the right thigh and on the scalp. The eruption was asymptomatic. Three months ago he had a peritonsillar abscess which was incised and drained. His history is otherwise insignificant.

The eruption at this time consists of lesions spread widely over the chest and back, a few on the frontoparietal aspect of the scalp and one on the right hip, the remainder of the body remaining free. On the back the lesions are small and coin shaped, erythematous, with a faint bluish tinge, elevated above the skin, definitely circumscribed and firm on palpation. In several areas confluence has occurred, with the formation of variously sized, irregular, more elevated plaques, especially over the left scapula. There are no visible or palpable axillary or inguinal nodes, nor can the spleen be felt.

Histologic study, on July 12, 1934, of tissue from a lesion on the back, showed the following features: Scattered throughout the cutis, predominantly in the middle and deeper zones, were irregular foci of cellular infiltration. In some of these areas were small thin-walled vessels. In the upper part of the cutis there was a sparse perivascular cellular infiltration. The elements of the infiltration in the middle and deeper parts of the cutis were predominantly of the small lymphocyte variety. The chromatin fibers and granules of the nuclei could be made out, and in some of the areas a small round area of protoplasm was noted. Mixed among these cells were some nuclei of the endothelial variety. The blood vessels when noted were almost occluded by swollen nuclei. There was no special arrangement of these cells, with mitotic figures or any special changes of the surrounding cutis. The observations in this specimen appeared similar to those noted in the lymphadenoses and similar conditions.

The Wassermann reaction of the blood was negative. A blood count showed 90 per cent hemoglobin and 4,500,000 erythrocytes and 8,800 leukocytes per cubic millimeter, with a differential count of 37 per cent polymorphonuclear leukocytes, 52 per cent lymphocytes, 3 per cent large mononuclear leukocytes, 5 per cent eosinophils, 1 per cent basophils and 2 per cent myelocytes.

Therapy consisted of a total of seven skin units (2,100 r) of roentgen rays over the affected areas during five months. No single lesion received over two skin units, however, and all roentgen rays were unfiltered. The lesions responded favorably to this therapy, but the patient failed to return. He was not seen again until April 17, 1940, after having received interim roentgen therapy from another physician. At this time he presented on the anterior wall of the chest a deep ulcer with an elevated, cartilaginous-like border, oval, approximately 5 by 4 inches (13 by 10 cm.) in diameter. Its base was ulcerated, moist and granular in appearance. The lesion was sharply marginated. Adenopathy was not more pronounced than in a normal person except that the epitrochlear glands were pea sized, hard and difficult to palpate.

Microscopic examination showed a tremendous cellular infiltrate, partly focal and partly diffuse. The cells were all large, with large oval hypochromatic nuclei and definite cell bodies. Some of the cells were multinucleated, suggesting Sternberg cells. There were some mitotic figures. At another edge of the section the vessels were dilated, and about them was a definite cellular infiltrate composed of small round cells. The epidermis showed no important changes. The histologic diagnosis was lymphoblastoma, suggestive of Hodgkin's disease.

The blood count at this time showed 90 per cent hemoglobin and 5,350,000 erythrocytes and 8,900 leukocytes per cubic millimeter, with a differential count of 5 per cent nonsegmented and 61 per cent segmented polymorphonuclear leuko-

cytes, 25 per cent lymphocytes, 4 per cent monocytes and 5 per cent eosinophils. The platelet count was 250,000 per cubic millimeter. A roentgenogram of the chest was normal.

DISCUSSION

DR. J. FRANK FRASER: Because of the apparent origin of the lesion in the skin I should not entertain the diagnosis of lymphoid leukaemia cutis. The fundamental changes in that disease begin in lymphoid tissue. There is no evidence of involvement of the lymph nodes in this case. On the other hand, the fact that the lesion is in the true skin and the gross appearance are suggestive of mycosis fungoides. Mycosis fungoides is primarily a cutaneous disease, and the occurrence of adenopathy is a secondary phenomenon and theoretically may never supervene. From a brief examination of the slide presented, I feel that this case should be recorded as an example of mycosis fungoides of the d'emblée type.

DR. EUGENE F. TRAUB: From clinical inspection I should say that the lesion on the abdomen presents about as classic a picture of what is called mycosis fungoides as anything could. It is a crescentic or horseshoe-shaped lesion and in a location, strangely enough, where one is particularly accustomed to see this type of lesion. From the points mentioned by Dr. Fraser and from the fact that the patient is still alive and well nine years after the first appearance of the condition, I should say that the disease is a slowly progressive d'emblée type of mycosis fungoides. I recall a patient with an identical lesion on the abdomen, in whom a great many of these lesions developed as time went on. They all disappeared as a result of roentgenotherapy and were replaced by a large number of tumors which were histologically lymphosarcoma. I think the picture both clinically and microscopically may be definite in these cases.

DR. HANS J. SCHWARTZ: I agree with the clinical diagnosis of mycosis fungoides.

DR. A. BENSON CANNON: I, too, thought mycosis fungoides the most likely diagnosis, but one should not lose sight of the possibility of the lesion's being sarcoma.

DR. GEORGE C. ANDREWS: I agree with Dr. Traub's conception of the case.

DR. J. GARDNER HOPKINS: I think the condition is mycosis fungoides. I should like to ask Dr. Fraser if he did not think that the cells were larger than those ordinarily seen in leukemia. The cells also seemed more uniform than they are usually in mycosis fungoides. Is the histologic picture of mycosis fungoides with tumors at the onset a little different perhaps from that of the typical example of the disease in the third stage?

DR. J. FRANK FRASER: In answer to Dr. Hopkins' question, the cells in this section are reticular and longer or larger than the lymphoid cell of lymphatic leukemia.

DR. R. H. RULISON: Would there be any advantage in making a complete excision of this lesion and then grafting skin?

DR. J. FRANK FRASER: Surgical excision is contraindicated. Roentgenotherapy is preferable.

DR. PAUL E. BECHET: I agree with those who feel that the condition in this case is mycosis fungoides. The lesion on the back which is not ulcerated is infiltrated and suggests mycosis fungoides. Another point which is in favor of that diagnosis is that the lesions were particularly sensitive to roentgenotherapy.

DR. HOWARD FOX: The former lesions on the back and the one now present on the abdomen are probably the same disease. From the clinical appearance and from the histologic and serologic studies that have been made, one can exclude syphilis, tuberculosis, carcinoma and sarcoid. The probable diagnosis of lymphoblastoma remains by exclusion. The extreme sensitivity of the former lesions on the back to roentgen rays favors this diagnosis. I also understand that the lesion on the abdomen has probably received an inadequate amount of roentgen rays. Mycosis fungoides is, I think, the most likely diagnosis.

DR. GEORGE C. ANDREWS: Although mycosis fungoides is usually regarded as a systemic disease, I think, as Dr. Fraser said, that it primarily begins in the skin and that if one treats the original d'emblée lesion effectively, there is a chance to stop the process. I base that conclusion on a case similar to the one mentioned by Dr. Fraser. The patient had a d'emblée type of mycosis fungoides on the abdomen. The condition was seen by Dr. Satenstein and others and definitely accepted as such. He was presented before the Manhattan Dermatologic Society (ARCH. DERMAT. & SYPH. **33**:182 [Jan.] 1936). I treated the ulcer with a heavy dose (8 erythema doses) of roentgen rays, filtered through 3 mm. of aluminum. Atrophy developed at the site of the lesion. The lesion at the time of treatment was a large ulcerated tumor, measuring about 4 inches (10 cm.) in diameter, and it was the only lesion present. He remained entirely free from lesions for eight years, and then pruritic infiltrated patches developed on the thighs.

DR. FRED WISE: I assume that all dermatologists have encountered so-called borderline conditions like this one, a definite diagnosis of which is not arrived at either with the aid of the microscope or by any other means. A lesion on the abdomen such as this may occur in three conditions, namely, mycosis fungoides—the diagnosis I favor in this case—lymphatic leukemia and sarcoma.

Leprosy (Mixed Type). Presented by DR. HOWARD FOX.

C. S., a man aged 39, was previously presented in January 1938 (ARCH. DERMAT. & SYPH. **38**:100 [July] 1938). Since the last presentation the eruption has become more profuse and now shows an unusual geographic configuration. It is situated mainly on the anterior, lateral and posterior aspects of the trunk, to a lesser degree involving the buttocks and thighs. The eruption consists of annular lesions varying in diameter from 2 to 10 cm. The average width of the borders is about 1 cm. The borders are salmon colored, definitely infiltrated and slightly elevated above the surface of the skin. The central parts of the lesions are paler than the normal skin. In the center of some of the rings there are solid plaques of varying size and of the same color as the borders. Both the borders and the centers are anesthetic to the prick of a pin. Some of the lesions have coalesced and formed gyrate patterns. During the past two years the involvement of the hands has increased in severity. Two of the fingers were amputated for intractable swelling and ulceration.

Histologic examination of the border of a lesion on the trunk was made by Dr. D. L. Satenstein, who gave the following report: "Throughout the upper part of the cutis are many collections of the histiocytes in tubercle formation. About these is a moderate cellular infiltrate. In the remainder of the cutis there is some parenchymatous edema. Otherwise there is no change. The epidermis is comparatively thin, and in some areas the rete pegs and papillary bodies are missing. The tubercles are in part isolated and in part arranged in bandlike fashion. The histiocytes composing these masses have a granular or foamy cytoplasm, and the outlines are broken up. No organisms were found."

DISCUSSION

DR. FRANK C. COMBES: I was interested in the probability of a tuberculoid structure in these lesions. I was always under the impression that these cutaneous lesions of neural leprosy were of the vascular type and did not show any infiltration whatever, that is, that they were more or less identical with the lesions of a neurosyphilid.

A Case for Diagnosis (Acanthosis Nigricans?). Presented by DR. FRED WISE.

Miss F. I., aged 36, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on March 14, 1940, complaining of a dark brown discoloration on the face, which had first appeared three years ago. Her general health had always been good. She had always had a dark complexion and tanned readily. About three years ago, two teeth were extracted from the

left side of the upper jaw "because of a cyst." On the day after the extraction the left side of the face was swollen and inflamed. Approximately two months later dark brown spots appeared on the skin adjacent to the nose and on both cheeks, chiefly affecting the skin around the mouth and the lateral aspects of the chin. She was admitted to the New York Hospital for examination on May 30, 1938. There a complete physical check-up disclosed no significant deviations from normal health.

Examination shows an area of dark brown pigmentation on both sides of the midportion of the nose, an inch (2.5 cm.) above the alae nasi, and broad areas of hyperpigmentation around the mouth, extending from the nasolabial folds toward the lobes of the ears and involving the lateral aspects of the chin. The surface of the affected areas is soft to the touch but has a definitely rugose appearance, resembling finished pigskin. There also appears to be a faint periorbicular hyperpigmentation but without apparent alterations in the surface of the skin in these areas. The borders of the peribuccal lesions are ill defined on the cheeks and chin, and the color fades out toward their peripheries.

Histologic examination of a section of hyperpigmented skin showed "melanosis, probably preceded by an inflammatory process" (Dr. D. L. Satenstein and Dr. Wilbert Sachs).

DISCUSSION

DR. EUGENE F. TRAUB: I suggest the possibility of acanthosis nigricans, because of the slight changes in the axillas. I thought the skin was not merely pigmented but thrown into verrucous folds and thickened. I do not think the condition is an ordinary pigmentary disturbance of the skin but one associated with some internal constitutional disease.

DR. A. BENSON CANNON: I have 2 patients under treatment for a pigmented condition exactly like that in this patient, a condition I have found to be due to the use of a commercial eau de cologne. The location, distribution and character of the pigmentation all favor a cosmetic as being the most likely cause. One of my patients had been thoroughly peeled on two occasions, first at a beauty parlor and later by a dermatologist, and in the first instance the condition was much aggravated. I find that such pigmented areas in women are not uncommon. I have had the most success by the use of remedies that cause a slight desquamation of the skin without producing too much local irritation. The character of the pigmentation in this case in no way resembles that seen after the taking of phenolphthalein, and I should discount that drug as being a possible cause.

DR. GEORGE C. ANDREWS: I do not feel that this case is one of perfume dermatitis, because the color is too dark, being a slate color, which is the color of a phenolphthalein reaction. I asked the patient if she took any laxatives, and she said she did occasionally. I asked her what type of laxative she took, and she replied "ex-lax" and magnesia magma. The other two suggestions of acanthosis nigricans and perfuse dermatitis should, of course, be kept in mind.

DR. R. H. RULISON: I was with Dr. Andrews when the history of ingestion of phenolphthalein was obtained. I favor the diagnosis of acanthosis nigricans because of the verrucous nature of the eruption.

DR. PAUL E. BECHET: It seems to me that there are definite points against the diagnosis of a phenolphthalein eruption. These are the absolute symmetry in distribution, the tremendous pigmentation (almost black), the velvety papillomatous growth and the apparent lack of any cutaneous or subcutaneous inflammation. While I have, of course, seen phenolphthalein eruptions which were dark, they were, however, of a dusky brownish red and never black. I do not believe that the condition is due to a chemical reaction from cosmetics. The evidence in favor of the diagnosis of acanthosis nigricans of the juvenile type is not convincing, but the suspicion remains. If the same degree of pigmented, velvety, rugose papillomatosis occurred in the axillas or beneath the breasts, that diagnosis would immediately suggest itself. After weighing the clinical evidence carefully, one cannot completely dismiss this suspicion.

DR. HOWARD FOX: This eruption is not solely a hyperpigmentation. There is evidence of inflammation and unquestioned thickening of the skin. The condition is certainly not argyria or, in my opinion, an eruption due to phenolphthalein. The latter condition occurs in patches which are fairly well demarcated and which do not fade into the surrounding normal skin as do the lesions in this case. If the lesions had been present in the axillas, no one would have questioned the diagnosis of acanthosis nigricans. However, I have never seen this disease on the chin or cheeks and feel doubtful about the diagnosis.

DR. A. BENSON CANNON: Will Dr. Wise comment on the apparent good health of this woman for one who has acanthosis nigricans following a carcinoma?

DR. GEORGE C. ANDREWS: I have seen thickening of the skin due to rubbing in cases of phenolphthalein eruption. I admit that the thickening here does not look like lichenification. The condition has the velvety appearance of acanthosis nigricans, it is true, but the more common disease would be an eruption due to phenolphthalein, and she gives a history of having taken phenolphthalein.

DR. FRED WISE: I have never observed any phenolphthalein eruption resembling this condition, with respect to either color or conformation, and I should discard that tentative diagnosis. As to general health, I think most patients with early manifestations of acanthosis nigricans who have no visceral lesions are apparently in good health.

Extensive Acrodermatitis Chronica Atrophicans in a Man. Presented by DR. PAUL E. BECHET.

H. E., a man aged 50, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on April 16, 1940, complaining of tightness of the skin of his feet and legs. The eruption began twenty-two years previously on the dorsal surfaces of the feet. During eighteen years the condition spread slowly but steadily, until the entire lower extremities from just above the lumbosacral region of the back to the toes present a symmetric involvement. There has been no change in the eruption in the past four years. The surface of the skin is glossy, atrophic and hairless. There are areas of telangiectasia, and the surface blood vessels are prominent beneath the thinned integument. Several areas are atrophic, and others suggest sclerodermatous changes, particularly about the ankles and dorsal surfaces of the feet. The Wassermann and Kahn reactions were negative. The urine was normal. The histologic report agreed with the clinical diagnosis.

DISCUSSION

DR. HOWARD FOX: Though this disease usually occurs in women, it also affects men occasionally, as in a patient of mine previously presented before this society (ARCH. DERMAT. & SYPH. **24**:1129 [Dec.] 1931). The disease does not seem to shorten life or affect the general health. However, it may cause a good deal of annoyance or even disability from ulcerations, especially over the malleoli, where the skin is tightly stretched and easily traumatized. Such ulcerations are apt to last for many months and constitute the only serious feature of the disease.

Cheilitis. Presented by DR. EUGENE F. TRAUB.

H. Z., a youth aged 19, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on March 11, 1940, with an eruption about the lips of two and one-half years' duration.

Examination shows about the lip a well defined, erythematous, edematous, fissured, slightly crusted and scaly circumscribed patch. The right inner surface of the lower lip shows a raised oval lesion. There is an ill defined macular eruption about the tip of the nose extending downward to the sides and involving the nasolabial folds. The tongue is smooth, erythematous, enlarged and fissured. About the index and middle fingers, which are symmetrically involved, especially on the right hand, there is an ill defined erythematous thickened, lichenified and scaly patch on the inner surfaces. There are moderate scaliness and maceration between the fourth and fifth toes.

The patient smokes Philip Morris cigarets and uses Dr. Lyons' tooth powder. He eats a well balanced diet. Patch tests were made with Philip Morris cigaret paper and gave negative results, but tests with Philip Morris tobacco gave positive results. Patch tests were also made with Pall Mall cigaret paper and tobacco, but the results have not yet been read. The Wassermann and Kahn reactions were negative.

Leprosy with Juxta-Articular Nodes. Presented by DR. FRED WISE.

In October 1939 I presented a woman with leprosy associated with large juxta-articular nodes at the elbows (ARCH. DERMAT. & SYPH. **41**:789 [April] 1940). At that time several members said they did not think the nodules around the elbows were manifestations of leprosy. Strange to say, the injections of chaulmoogra oil partly cleared up the cutaneous lesions and caused considerable diminution in the size of the nodules.

Leukemia of the Skin. Presented by DR. EUGENE F. TRAUB.

E. D. was previously presented before the Atlantic Dermatologic Conference on March 9, 1940 (ARCH. DERMAT. & SYPH. **42**:687 [Oct.] 1940) with typical leukaemia cutis with bullous lesions in some areas and solid masses in others. The condition was thought by some of the members to be leukemid rather than true leukaemia cutis. To confirm or refute this supposition, several biopsies were performed, with one specimen from an area on the vulva and another specimen from a lesion on the arm. The histologic diagnosis was leukaemia cutis.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

E. WILLIAM ABRAMOWITZ, M.D., *Chairman*

LEWIS B. ROBINSON, M.D., *Secretary*

May 7, 1940

A Case for Diagnosis (Mycosis Fungoides?). Presented by DR. ABRAHAM WALZER.

M. S., a woman aged 32, is presented from Beth Moses Hospital. The past history is irrelevant. An eruption began four or five years ago with the development of three small spots, one on the right cheek, one on the left breast and one on the left forearm. Within three months the eruption had become widespread, covering the upper and lower extremities and the trunk in irregular patches of papulovesicular oozing dermatitis. She was treated in various local institutions with external and internal medication. The condition never completely cleared up; faintly brownish pigmented spots remained. For six months the patient was fairly well, with only a small spot here and there. Since then she has had numerous outbreaks, but none has been as serious as the first one.

The present eruption is of about one year's duration. The lesions are limited to the right cheek, the right arm and both breasts, particularly in the areolar areas. The trunk and extremities show many faintly pigmented patches of various sizes, the remains of previous lesions. The elementary lesion is a small pruritic papule or papulovesicle, varying in size from that of a pinhead to that of a lentil. These papules combine into patches forming oozing, elevated lesions from the size of a dime to that of a quarter. In some locations these lesions are arranged in semiannular formation (on the right arm). Some of them are covered with an impetiginous crust, while others have a papillomatous surface.

Complete physical examination showed no abnormalities aside from the cutaneous condition. The liver and spleen were not enlarged, but the axillary nodes were somewhat enlarged. The Wassermann reaction was negative. The

urine was normal, and the blood count on various occasions was also normal. Studies of the bone marrow showed no abnormality. Smears from the lesion on the breast showed no fungi.

Histologic examination of a specimen taken from the lesion on the breast showed acanthosis of the epidermis, especially of the rete pegs, and small and large vesicles in the upper layer of the epidermis. The basal cell layer was intact. Mitotic figures were scattered throughout. In the cutis there was dilatation of the vessels, with interstitial edema and an infiltration of pleomorphic cells, consisting of round cells, plasma cells, histiocytes, eosinophils and large reticular cells.

DISCUSSION

DR. J. FRANK FRAZER (by invitation): On the basis of the histologic picture, before I saw the patient, I had concluded that the condition might be mycosis fungoides. After seeing the patient I am willing to admit that the gross appearance of the lesions does not harmonize with that view. Nevertheless, I still favor the diagnosis of mycosis fungoides.

DR. FRED WISE: I suggest careful, repeated bacteriologic examinations.

DR. HERMAN GOODMAN: Did the patient present a generalized eruption which cleared up spontaneously?

DR. ABRAHAM WALZER: The disappearance was not spontaneous.

DR. HERMAN GOODMAN: What treatment was effective?

DR. ABRAHAM WALZER: Treatment consisted of many types of applications.

DR. HERMAN GOODMAN: Did the condition clear up under roentgenotherapy?

DR. ABRAHAM WALZER: The lesions did not respond to roentgenotherapy.

DR. GEORGE C. ANDREWS: I should like to ask Dr. Walzer how much roentgenotherapy this patient had. What were the dosage and the intervals?

DR. CHARLES WOLF: At present any diagnosis would be speculative. So far, none of the features of a lymphoblastoma have been revealed, and the only suggestive feature is the microscopic picture. However, the clinical aspects are diametrically opposite to what is to be expected in any of the lymphoblastoma group. The diagnosis of mycosis fungoides has been made tentatively. None of the features seen in that condition has been noted in a period of five years. The itching is slight, and there is no infiltration. Thirdly, the lesions are bullous. Furthermore, the response to roentgen rays is one of the specific phenomena in mycosis fungoides or leukemia. The leukemic picture here is also all on the negative side. Puncture of the marrow gave negative results, and the blood picture has been consistently normal. The lesions do not appear to be those of leukemia or of leukemid. Hodgkin's disease certainly does not produce phenomena as seen in this case. The clinical picture is of a circinate, papulovesicular eruption which clears intermittently and does not produce any systemic disturbances. I therefore suggest the diagnosis of chronic erythema multiforme or, possibly, dermatitis herpetiformis.

DR. DAVID L. SATENSTEIN (by invitation): The clinical features, the microscopic picture and the history do not fit in with any diagnosis mentioned. Dr. Eller's case of iododerma tuberosum is no doubt familiar. The history and the clinical and histologic pictures suggest iododerma.

DR. J. FRANK FRAZER (by invitation): Dr. Satenstein just stated that he saw nothing in the histologic picture that looked like mycosis fungoides. I should like to know how he interprets the nests of reticular cells with hyperchromatic nuclei and mitotic figures which dominate the picture.

I recall Dr. Eller's case. I opened the discussion on it when Dr. Eller read his report before the American Dermatological Society. I stated then that the histologic picture was "exactly the same as that seen in the tumor stage of mycosis fungoides" (ARCH. DERMAT. & SYPH. **24**:777 [Aug.] 1931). This view was not challenged. Dr. Wile in discussing the case said he was "entirely in accord" with my view. He also stated that he did not think that the case was a true iododerma.

DR. ABRAHAM WALZER: This patient has been under observation for over four years. She refused to permit a biopsy for a long time and therefore continued to visit various institutions without receiving any definite diagnosis. Answering Dr. Goodman's question about therapy, I meant that I used all the ordinary remedies employed in various clinics, such as ointments, pastes, dyes and lotions, giving them at various intervals. There was no apparent immediate result. The lesions would eventually clear up, and the last treatment she had had was credited with the cure, but the condition always recurred. Concerning the question of roentgenotherapy, I did not give her any. Before she returned to the Beth Moses Hospital seven months ago she had been treated by a roentgenologist in Brooklyn, who gave her four treatments at weekly intervals, without any apparent results. The question of pruritus has been raised. She has itching, as is evidenced by scratch marks, though it is not as intense as one would expect in mycosis fungoides. In my tentative diagnosis of lymphoblastoma, I excluded Hodgkin's disease, leukemia and lymphosarcoma. I suggested mycosis fungoides tentatively because a pathologist suggested the possibility of Hodgkin's disease. Mycosis fungoides, if it is a lymphoblastoma, is a primary lymphoblastoma of the skin. On the other hand, Hodgkin's disease is an internal disease, and the lesion of the skin is secondary. Therefore, if this condition were Hodgkin's disease, one would expect internal involvement. If it is mycosis fungoides, it is in the prefungoid stage, before infiltration has occurred, and one would not expect any of the internal manifestations of mycosis fungoides now; they occur at the terminal stage, if at all. As to the ingestion of iodides and bromides, I went into that question carefully. I suspected drugs, especially iodides. She states that she has not taken any drugs. She was warned not to take any. She recently refused to take capsules which her physician prescribed for a cold. Mycosis fungoides can exist in such a stage for twenty-five years, so that the question of time does not enter into the discussion. I still think that clinically the condition is certainly not mycosis fungoides, but the histologic picture suggests it. About the question of a bacterial investigation, numerous smears and cultures were made, but only some nonpathogenic organisms were obtained.

A Case for Diagnosis (Erythema Multiforme?). Presented by DR. JACOB SKEER (by invitation).

D. C., a woman aged 43, is presented from Cumberland Hospital, for Dr. David M. Davidson. The eruption began five years ago in the fall of the year and then cleared up. There was a recurrence the next year, and then the lesions again disappeared. For the past three years there have been recurrent crops of lesions, which have not cleared up completely. The eruption began on the ankles and spread upward to involve the legs, thighs, abdomen and breasts.

Examination shows numerous circinate and gyrate lesions with vesicular and bullous borders and flat erythematoviolaceous centers. The itching is severe and at times intolerable. The patient states that the eruption is aggravated or improved according to the weather, being more severe in damp and rainy periods. The eruption appears in crops, with remissions every two weeks.

The Wassermann reaction was negative. The urine was normal. Chemical examination of the blood showed 93 mg. of sugar, 12.5 mg. of urea nitrogen, 1.4 mg. of creatinine and 3.4 mg. of uric acid per hundred cubic centimeters. A blood count showed 82 per cent hemoglobin and 4,000,000 erythrocytes and 9,700 leukocytes per cubic millimeter, with a differential count of 67 per cent neutrophils, 3 per cent eosinophils, 25 per cent lymphocytes and 5 per cent mononuclear leukocytes. Examination for tinea gave negative results. A patch test with potassium iodide gave negative results. The histologic diagnosis was erythema multiforme.

DISCUSSION

DR. EUGENE T. BERNSTEIN: I consider this case to be one of erythema multiforme, not of the Hebra variety, due to ingestion of some drug. The patient claims that she took a bromide.

DR. DAVID M. DAVIDSON (by invitation): I was unable to obtain a history of ingestion of drugs. According to the record, the patient was treated once with strontium bromide. The condition did not become worse, nor did it improve much.

DR. E. WILLIAM ABRAMOWITZ: Regarding a history of drug ingestion, the patient volunteered that she had been taking all kinds of bromide preparations in the past but none recently. It is known that a bromide eruption can appear long after administration of the drug is discontinued. There is still a possibility that this condition may be a drug eruption. Has an analysis of the urine for bromides or iodides been made in this case? If not, I think that it should be and that the patient should receive intensive sodium chloride therapy.

DR. FRED WISE: For what was she taking bromides?

DR. E. WILLIAM ABRAMOWITZ: She said she was taking the bromides for some kind of nervous spells. I asked her about using iodized salt, and she said she had not used any. She is well informed on the subject, perhaps so much so that her eruption may be induced.

DR. JACOB SKEER (by invitation): If this woman appears well informed, she has received all her information from my associates and me. We also suspected a drug eruption and cautioned her against taking any drugs. We do not know whether she has taken any drugs, but as far as we can find out, she has not. The strontium bromide was given at the hospital for the itching and sleeplessness, and she seemed to feel better after it. Any drug she has had has been taken since the onset of the eruption.

Hypertrophic Scarring Following Eczema Vaccinatum. Presented by DR. JACOB SKEER (by invitation).

M. B., a woman aged 40, is presented from Cumberland Hospital, for Dr. David M. Davidson. The patient states that an eczematous eruption developed on her neck about the middle of January 1940, presumably caused by a new sweater. The eruption then spread to the upper part of the chest and the arms. Three weeks later her two children were vaccinated. About eight to ten days later, blisters appeared on the patient's neck, and she applied to the Emergency Room of the Cumberland Hospital for treatment on February 16. The skin of the neck and arms was an angry red, and numerous vesicles were present. Her temperature was 100 F. She was sent to Kings County Hospital and was transferred to the Kingston Avenue Hospital. On admission she presented, according to the records, a vacciniform eruption consisting of numerous scattered, discrete and confluent, umbilicated pustules surrounded by an erythematous areola, situated on the neck, the upper part of the chest and the arms. The temperature was 105 to 106 F. There was a submaxillary and cervical adenitis. The blood count showed 4,300,000 erythrocytes and 12,000 leukocytes per cubic millimeter. The urine was normal. The temperature remained at 105 to 106 F. for nine days, after which it fell to 100 F. and then became normal in four days. The patient remained in the hospital for six weeks and was then discharged. She states that she was vaccinated during childhood but it "did not take." There was no vaccination scar present.

Examination at the present time shows widespread hypertrophic erythematous scarring, involving the neck like a collar and the upper part of the chest. On the arms and chest are numerous hypertrophic and atrophic scars, the sites of the vacciniform lesions. Movement of the neck is inhibited and limited, owing to the scarring.

DISCUSSION

DR. ABRAHAM WALZER: I treated this patient for almost seven weeks at the Kingston Avenue Hospital. She had a high temperature, and there was a suspicion at one time of smallpox. The question of eczema vaccinatum is interesting, because there seems to have been an increase in its incidence in the past few years. At least, I have encountered 5 or 6 cases in the last year or two. It was first described in 1887 by Kaposi, who thought it was due to a fungous infection. A few years

later Juliusberg described it under the name pustular vacciniform eruption. At present this condition is included under postvaccinal eruptions. There are a number of types of such eruptions. One represents the hematogenous spread of the virus from the site of vaccination, causing true generalized vaccinia. Occasionally attacks of urticaria or erythematous eruptions which are also due to dissemination of the virus are encountered. Another type is due to the spread of the virus from one site to another, or contact infection, such as occurs when a child touches the site of vaccination and then touches another part of the skin, close by or far away. Here a group of these vacciniform eruptions develops. The third type is that in which there is an introduction of the virus into the system through a diseased site, as in this instance. That is serious. The mortality is about 50 per cent. That is one reason why infants with eczema should not be vaccinated or allowed to be near people who have been vaccinated. When the virus gets into such an eczematous lesion, it is said that there is a tremendous increase in local production of the virus, and the system is overwhelmed under this high dose, with a resulting terrific reaction, such as this woman had. There is the fourth type, in which there is secondary infection on top of a vaccination, such as impetigo. Tuberculosis and even syphilis have been described. There is still another type, which probably should not be included here but which is described with postvaccinal eruptions. Occasionally lichen planus will develop in a child after a vaccination, or pemphigus or psoriasis, but those, of course, have nothing to do with this case. At the Brooklyn Jewish Hospital about ten days ago I saw a 6 month old baby with this condition who died.

DR. SEYMOUR H. SILVERS: I saw this patient at the Kings County Hospital before she was sent to the Kingston Avenue Hospital. In fact, I was responsible for her transfer. The lesions I saw were those usually seen in vaccinia. In vaccinated children, first a papule is observed, and then a vesicle, followed by a pustule, ulceration and crusting. This patient showed lesions in these various stages over the body, but on the neck there was a gangrenous mass. I believe that while she was at the Kingston Avenue Hospital she received either sulfanilamide or sulfapyridine. She has lost a great deal of weight since I first saw her.

DR. ADOLPH ROSTENBERG: I have no doubt that this case is one of eczema vaccinatum due to accidental contact with the children who had been vaccinated. I remember a boy with an eruption similar to this and with constitutional symptoms, and he died. The keloidal formation reminds me of a patient presented a few weeks ago with keloid formation following herpes zoster. I think in these deep destructions keloids develop, perhaps, in persons who have a tendency toward keloid formation.

DR. E. WILLIAM ABRAMOWITZ: Has Dr. Rostenberg any suggestions for treatment?

DR. ADOLPH ROSTENBERG: The only suggestion I have for treatment is roentgenotherapy; it should have been started early.

DR. EUGENE T. BERSTEIN: I should like to suggest a possible explanation for the development of these hypertrophic or keloidal scars. The patient had severe itching and scratched herself a great deal, and through this trauma these keloidal scars developed.

DR. DAVID M. DAVIDSON (by invitation): I should like to hear more suggestions for therapy. The most important thing to me now is what to do with this patient. Is the problem one for roentgenotherapy or for plastic surgery?

DR. ABRAHAM WALZER: In answer to Dr. Silvers, this woman received sulfapyridine for five days but became cyanotic and showed other toxic symptoms, and its administration had to be stopped. As for the hypertrophic scars or keloids, I do not believe one can incriminate any treatment or any type of trauma. I believe it is an inherent tendency. In a certain percentage of people keloids or hypertrophic scars develop no matter what the type of treatment or type of injury has been. This woman has this tendency to keloid formation.

DR. HERMAN GOODMAN: This woman has no keloids. She had injuries down to the true skin. There are eight or nine depressed areas on the chin. The edge of the normal skin is higher than the places where the skin was injured by the vaccinia. If she had a tendency to keloid formation, every injury to the true skin should show a raised lesion. She had a gangrenous-like eruption which led to the exposure of the deeper tissues. The resulting scars contracted and pulled the face and chin down to the neck. She has a contracting scar of the neck. No hypertrophic scars are visible in places where the true skin was injured.

Senile Elastosis. Acrodermatitis Chronica Atrophicans. Presented by DR. ABRAHAM WALZER.

M. C., a man aged 63, is presented from Brooklyn Jewish Hospital, complaining of an eruption of many years' duration, involving the face, neck, ears, trunk and lower extremities. The patient is a carpenter. He first came to the clinic a year ago, complaining of an infection on his right cheek, of pigmented patches on the face and neck and of lesions on the lower extremities.

Examination shows the scar on the right cheek resulting from the infection. The pigmented patches he complains of are seen on the back and sides of the neck, in the eyebrow area, on the skin adjacent to the inner canthus of each eye and on the helix and anthelix of each ear. The color varies from ivory white on the ears and in the eyebrow area to yellow on the neck. The white areas are smooth, soft, sharply outlined and not elevated or only faintly elevated. The patch on the neck feels thickened but soft, and the natural cutaneous folds are accentuated. There is no suggestion of a papule as the elementary lesion, although there are a few scattered pigmented points (level with the skin) surrounding the patch on the neck. The skin of the face is thinned, with the vessels shining through. On the posterior part of the hard palate and on the soft palate is a patch composed of telangiectatic points on a yellow pigmented surface. The sides of the tongue are also tinged light yellow.

On the lower half of the trunk and on both lower extremities, extending to the toes, is an extensive diffuse atrophic dermatitis. All stages of this dermatitis can be seen, from bright red to dusky blue erythema and from raised, inflammatory boggy patches (lumbar region) to thin, wrinkled skin. The subcutaneous veins stand out prominently.

The icteric index and the values for total and free cholesterol and for sugar were within normal limits. A section taken from the lesion on the neck showed atrophy of the epidermis, with flattening and disappearance of the papillae. Immediately beneath this was a mass of degenerated elastic tissue extending across the section in a bandlike area. The elastic fibers were thickened, broken and twisted. The blood vessels and appendages showed no changes.

Pseudo Xanthoma Elasticum with Angioid Streaks of the Retina. Presented by DR. SEYMOUR H. SILVERS.

A. D., an unmarried man aged 43, residing in the United States for the past seventeen years, is presented from Beth Israel Hospital, complaining of generalized itching of two years' duration and of imperfect vision.

Examination shows a well developed man who presents on both sides of the neck, extending to the face and down to the clavicles, ill defined patches devoid of hair and having a velvety texture. The color varies, ranging from light yellow to lilac. The follicular openings are prominent. Definite papules cannot be felt. The left axilla shows a similar velvety patch about the size of a palm, which is also devoid of hair but is grayish white. A similar patch is present in the right axilla.

Examination of the retina shows numerous hemorrhagic streaks. Varying retinal lesions resulting from former hemorrhages have been seen at previous examinations. The patient's vision is gradually diminishing, and he is unable to follow his trade as a cook.

A blood count was normal except for eosinophilia (9 per cent eosinophils). The urine was normal. The Wassermann and Kahn reactions were negative. The amounts of dextrose, urea, nonprotein nitrogen, calcium and cholesterol in the blood were within normal limits. There were no parasites in the stool. Roentgen examination of the bones failed to show Paget's disease . The arteries of the legs showed calcification. Histologic examination of a section of skin showed typical pseudo xanthoma elasticum.

DISCUSSION OF PAPERS BY DR. WALZER AND DR. SILVERS

DR. SEYMOUR H. SILVERS: In this condition, the cutaneous lesions are only one part of the syndrome, which is known as the syndrome of Groenblad and Strandberg. The cutaneous lesions are the less important part of the syndrome. The more important part is the condition in the eye. The diagnosis of this syndrome was made by the opthalmologist at the hospital on examination of the fundi, before the skin was examined.

DR. HERMAN E. WOLFE (by invitation): I should like to say a word about the pathologic changes underlying the lesions of the retina. Between the retina and the choroid is a thin glassy membrane containing elastic tissue which is known as the lamina vitrea. In this membrane in this case the elastic tissue is destroyed, and cracks and fissures are produced. On looking into the eye with the ophthalmoscope these cracks or fissures are seen as gray to black to brown lacework, resembling vessels, which are neither in the choroid nor in the retina but somewhere between. These are the so-called angioid streaks. I have photographs here showing these streaks. There is a lacy network adjacent to the optic nerve which extends to the periphery. The retinal vessels are not involved in this particular condition. Lewis and Clayton (ARCH. DERMAT. & SYPH. **28**:546 [Oct.] 1933), however, reported that there was destruction of the elastic components of the vessels. That is probably so, since it is the only way to explain the hemorrhages which occur in the eyegrounds. The macula, which has to do with central vision, is usually involved. In this case, a mound projecting into the vitreous can be seen. This is due to hemorrhage, organized tissue and elastic tissue debris. The vision, of course, in this particular eye is completely lost and has been so for the past twenty-five years. In the other eye, subsequent examinations have disclosed small flame-shaped hemorrhages between the temporal arches. This indicates that the condition will follow the same relentless course as in the other eye.

An interesting feature is that frequently this condition is seen without pseudo xanthoma elasticum but rather with Paget's disease, which is an osteoporosis. What interested me in looking over the literature was this: In spite of the fact that pseudo xanthoma elasticum is comparatively rare, Dr. Goedblad of Leyden, in tracing back 67 cases, found angioid streaks associated with the pseudo xanthoma elasticum in 57 cases. This disparity interested me.

DR. E. WILLIAM ABRAMOWITZ: How many eyes examined post mortem have showed angioid streaks in the retina?

DR. HERMAN E. WOLFE (by invitation): About twenty-five eyes examined post mortem have showed this condition.

DR. JACOB SKEER (by invitation): Just as angioid streaks of the retina may occur without pseudo xanthoma elasticum, it is known also that pseudo xanthoma elasticum may occur without angioid streaks. A report made recently stated that angioid streaks of the retina accompanied pseudo xanthoma elasticum in only about 25 per cent of the cases (Sweitzer, S. E., and Laymon, C. W.: Pseudoxanthoma Elasticum, *Brit. J. Dermat.* **45**:512, 1933).

DR. ABRAHAM WALZER: Two conditions which are often confused histologically are pseudo xanthoma elasticum and senile elastosis. They are often difficult to differentiate. In pseudo xanthoma elasticum the fibrous bands are often in nodular formation and deep in the cutis, whereas in senile elastosis the picture is almost identical, but higher up, in the upper layers of the cutis. The clinical picture in senile elastosis is almost like that of pseudo xanthoma except that in the latter the elementary lesions are papules, because the lesion is a true elastoma—a true

elastic tissue tumor—whereas in senile elastosis there is no elementary papular lesion, since the increased amount of elastic tissue is not due to a production of new elastic tissue but only to a destruction of the connective tissue, which induces the elastic tissue to appear prominent. The lesion is, therefore, not an elastoma at all. As to the location of the lesions, in pseudo xanthoma elasticum the lesions are usually on the covered parts of the body, as for instance in the axillas and on the inner aspect of the arm, whereas in senile elastosis they are usually on the parts exposed to the elements. Pseudo xanthoma occurs early in life, while senile elastosis occurs usually after the age of 40. It is extremely rare to encounter 2 cases like these presented at a meeting together.

Xanthoma Diabeticorum. Presented by DR. SEYMOUR H. SILVERS.

D. S., a girl aged 15, is presented from King's County Hospital. She has been known to have diabetes for three years and has received approximately 30 to 40 units of protamine zinc insulin daily, with no restriction as to diet. About five months ago the patient noticed small white or pale pink pimples on her elbows. These gradually progressed in size, some coalescing to form small tumor masses, as they did on her lower extremities and buttocks, and persisting up to the present. She complains of polyuria and polydipsia. The past history is not significant except for the diabetes. Her family history is irrelevant.

Physical examination gave essentially negative results except for the cutaneous lesions. She is well developed and well nourished. There is hyperemia of the face. Situated around the elbows and other points of the body, as well as on the buttocks, are numerous bilateral and symmetric reddish yellow, pea-sized, discrete nodules.

Urinalysis showed a 4 plus reaction for sugar and a 1 to 4 plus reaction for acetone but no albumin. The Wassermann reaction of the blood was negative. Chemical examination of the blood showed 228 mg. of sugar, 22 mg. of urea, 1.17 mg. of creatinine and 296 mg. of cholesterol per hundred cubic centimeters. The plasma carbon dioxide amounted to 50 per cent. A blood count showed 75 per cent hemoglobin and 3,500,000 erythrocytes and 8,200 leukocytes per cubic millimeter, with a differential count of 45 per cent polymorphonuclear leukocytes, 52 per cent lymphocytes, 2 per cent monocytes and 1 per cent transitional forms. The basal metabolic rate was + 7 per cent. The icteric index was 4.5. A direct van den Bergh test gave a negative result. A test for bilirubin showed 0.2 mg. per hundred cubic centimeters of urine. Roentgenographic studies showed a small, shallow sella turcica, and internal hyperostosis of the frontal and parietal bones. The sinuses were small. There were no pulmonary or pleural changes. No abnormal mass or collection of fluid was seen in the abdomen. The observations were in line with cranial dysplasia, a form of hypopituitary disturbance.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: In view of the history of diabetes, with polyuria and polydipsia, and the bony changes, did Dr. Silvers consider the diagnosis of the Hans-Schiller-Christian syndrome?

DR. LOUIS TULIPAN: It appears to me that this condition is perhaps associated with some pituitary disturbance. I agree with what has been said. Some years ago I presented before this society a case of acromegaly with exactly the same picture (Tulipan, L.: Xanthoma Tuberosum Multiplex and Acromegaly, ARCH. DERMAT. & SYPH. **22**:724 [Oct.] 1930). Chemical examination of the patient's blood showed 500 mg. cholesterol and 364 mg. sugar per hundred cubic centimeters. A year after I saw him he returned to Bellevue Hospital, and there was not a sign of any lesion on the body, whereas before he had been covered with lesions. He had had absolutely no treatment during that year. The lesions disappeared spontaneously.

DR. SEYMOUR H. SILVERS: I think it has been accepted that diabetes may be either of pancreatic or of pituitary origin. In young patients one is likely to find pituitary changes on the roentgenogram of the skull. Diabetes in a young girl like this would more probably be of the pituitary type.

Alopecia Cicatrisata (Pseudopelade of Brocq). Presented by Dr. Abraham Walzer.

A. S., a married woman aged 42, is presented from Brooklyn Jewish Hospital with an eruption of the scalp of one and one-half years' duration. About twenty years ago the patient had an operation on the left mastoid, and two and one-half years ago she had an amputation of the cervix. The present trouble involves the scalp and extends from the temporal area to the region behind the mastoid on both sides. The patient says that these areas were never red or inflamed. The first thing she noticed was that the hair fell out slowly. At present these patches are white, glossy and faintly atrophic. No hair follicles are visible, and there are no "exclamation hairs" in the patches or in the borders. Hairs are scattered here and there in the bald areas.

Examinations of the hair for fungi and cultures of the hair showed no abnormalities. These observations were made on a section taken from the atrophic patch: There was a pronounced thinning of the epidermis with loss of papillae and complete absence of appendages. The collagen bundles were homogeneous, almost basophilic in staining affinity, and had completely lost their fibrillar character. Elastic tissue stain showed loss of the network in the subpapillary layers, but the elastic tissue in the deeper layers of the cutis appeared normal.

Alopecia Cicatrisata (Pseudopelade of Brocq). Presented by Dr. Abraham Walzer.

T. F., a woman aged 39, is presented from the Brooklyn Jewish Hospital with an eruption of the scalp of two years' duration. The past history revealed nothing of importance. The alopecia began on the vertex and gradually spread forward and to the sides. There was no soreness or pruritus associated with the loss of hair.

Examination shows numerous patches of alopecia varying in size from that of a pea to that of a dime or a little larger and arranged in linear or irregular formations, with areas of normal skin and hair between. The borders of the patches are irregular with distinct jutting out here and there. The surface of the bald spots is ivory-like in appearance, with complete absence of follicular openings. No broken hairs are seen. On palpation a faint depression can be noted.

Examination of the hair for fungi and cultures gave negative results.

DISCUSSION ON CASES OF ALOPECIA CICATRISATA

Dr. Max Scheer: The latter case was a typical one of alopecia cicatrisata, presenting pronounced atrophy without inflammatory evidence. The former, in my opinion, is not one of alopecia cicatrisata. There is no atrophy at all. The condition is just an alopecia (probably, I think, alopecia areata).

Dr. Adolph Rostenberg: I agree with Dr. Scheer. The characteristic feature in alopecia cicatrisata is the keratotic plug, which 1 of these patients showed but which was entirely absent in the other. In the second case the atrophy was pronounced, while in the first case the skin was smooth and showed no atrophy.

Dr. E. William Abramowitz: I should like to ask about the patient with patches on the sides of the scalp. This condition is frequently called alopecia ophiasique. Why does Dr. Walzer call it alopecia cicatrisata?

Dr. Max Scheer: I have had occasion to follow some of these cases of alopecia cicatrisata, and the earliest lesion is as typical as the one in the second case. Even a lesion that is no bigger than ⅛ or ¼ inch (0.3 to 0.6 cm.) in diameter already has a white milky appearance. One never sees a lesion enlarge to 1½ inches (4 cm.) in diameter in the early stage with a normal-appearing skin.

Dr. Abraham Walzer: One patient presents a typical example of this disease, but in the other the condition was only suggestive. For that reason, a section was removed for histologic study. I thought I saw faint depressions, and, in contradistinction to some of the discussion, there were definite areas with absence

of follicles. Of course, there were some hairs growing in the patch, and there were a few follicles noticeable. The histologic section showed distinct atrophy. Therefore, one must exclude alopecia areata, which never produces atrophy. So, because of the histologic picture and the peculiar clinical picture—the condition not being true alopecia areata—I feel that I am entitled to label the case one of pseudopelade of Brocq.

Lupus Vulgaris Disseminatus. Roentgen Ray Dermatitis? Pulmonary Tuberculosis. Presented by DR. GIRSCH D. ASTRACHAN (by invitation).

L. Q., a man aged 57, born in Austria, was admitted to Metropolitan Hospital on March 26, 1940. He was previously presented by Dr. George M. Lewis before the Manhattan Dermatologic Society on April 11, 1939 (ARCH. DERMAT. & SYPH. **40**:1065 [Dec.] 1939).

Since the previous presentation the blood count was found to be essentially normal. Chemical examination of the blood showed normal values for nonprotein nitrogen, sugar and creatinine, but the chlorides (as sodium chloride) amounted to 632 mg. per hundred cubic centimeters. The Wassermann and Kahn reactions of the blood were on one occasion weakly positive and doubtful, respectively, while one week later they were negative. The sputum showed tubercle bacilli. The tuberculin test in a dilution of 1 to 100,000 gave positive results. A roentgenogram of the chest (taken by Dr. Weinberg) showed probable caseous pneumonic tuberculosis, with cavitation in the right apex. Histologic examination (by Dr. Saccone) showed lupus vulgaris. The section showed small tubercles with giant cells of Langhans' type but no caseation.

DISCUSSION

DR. GIRSCH D. ASTRACHAN (by invitation): There are some interesting features in this case which I should like to mention. This patient had a weakly positive reaction to the Wassermann and Kahn tests of the blood on one occasion and a negative reaction the following week. This phenomenon may fit in with the well established fact that weakly positive nonspecific reactions occur in cases of tuberculosis. There is also a question as to the proper diagnosis of the ulcer on the right cheek. There is a possibility that the lesion is roentgen ray dermatitis, regardless of the fact that the most important symptom, namely, telangiectasia, is missing. Lupus vulgaris disseminatus usually appears in children following some xanthematic eruption. This factor is absent in this case. I feel, however, that because of the rapid development of the eruption on the back, this eruption can be called lupus vulgaris disseminatus. The case is presented mainly for therapeutic suggestions.

DR. CHARLES WOLF: It seems to me that the therapeutic approach in this particular case should offer no difficulty. Here is a man with active tuberculosis. His system is being fed constantly or periodically with streams of tubercle bacilli which are being disseminated. The thing to do here is to have the primary focus attended to, whether by pneumothorax, by removal of the patient to a high altitude or by generalized ultraviolet irradiation. I believe that systemic supportive treatment would prevent dissemination of tubercle bacilli from the pulmonary focus.

DR. HERMAN GOODMAN: Phthisiotherapeutists disapprove of giving a patient with active pulmonary tuberculosis any form of generalized irradiation. A nurse in a dermatologic clinic was given generalized ultraviolet irradiation without any previous examination. Acute pulmonary tuberculosis developed after one exposure.

DR. GEORGE M. LEWIS: While this patient was in the Neurological Hospital at Welfare Island, it was not certain that the ulceration on the right cheek was due to roentgen rays. However, the severe pain, for which he requested and received a large amount of sedatives, would indicate that the ulcer was due to roentgen rays even without the presence of telangiectasia. I believe it was the consensus at the time of the previous presentation that this lesion was a roentgen ray ulcer superimposed on lupus vulgaris. The roentgenotherapy was given in Vienna, Austria. He has consulted a great many physicians both here and abroad

and has had many forms of treatment, including gold therapy, salt-free diet and injections of a bismuth compound. No benefit from the therapeutic endeavors was noted; rest in bed had absolutely no effect. I think his condition is worse now than when I last saw him, eight or nine months ago. Sanatorium treatment is probably indicated, or perhaps, as Dr. Wolf suggested, a high altitude.

DR. E. WILLIAM ABRAMOWITZ: I should think that the prognosis in this case is poor now that there is beginning dissemination of the lesions. I had a patient with extensive lupus vulgaris of the face and neck following tuberculous mastoiditis (ARCH. DERMAT. & SYPH. **15**:351 [March] 1927). The lupus vulgaris healed completely under gold therapy. If this man has not had adequate gold therapy, I think it might be tried. There is nothing to lose.

DR. GIRSCH D. ASTRACHAN (by invitation): This patient did not respond well to applications of Aloe vera leaves. He claimed, however, that while he was on the salt-free diet his condition seemed to improve somewhat. I think that the advice of Dr. Wolf should be followed, that he should be given systemic treatment for the tuberculosis.

Erythema Figuratum (Erythema Annulare Centrifugum of Darier?). Presented by DR. ABRAHAM WALZER.

S. M., a woman aged 37, is presented from the Brooklyn Jewish Hospital, for Dr. David M. Davidson, complaining of an eruption of four months' duration on the neck, the trunk and the extremities. The past history revealed nothing of importance. The eruption began near the right elbow as a red pruritic spot. Four days later it spread, and many other lesions appeared and extended all over the aforementioned areas.

On March 20, 1940, nine weeks after the appearance of the eruption, the patient first presented herself at the clinic. She showed an eruption consisting of pruritic pinhead-sized to pea-sized erythematous papules with fine scaling to silver dollar–sized annular or elliptic lesions with raised erythematous borders and clearing centers, some with light brown pigmentation. At present many of the lesions have disappeared, leaving fine wrinkling or pigmentation. The most outstanding lesions remaining are on the side of the trunk and hips, where by coalescence they form many marginate and gyrate lesions with raised erythematous borders and light brown centers.

Repeated scrapings of the lesions and cultures have failed to show fungi. Histologic examination showed an acute exudative process compatible with that seen in the erythema multiforme group of diseases.

Darier's Disease (Keratosis Follicularis). Presented by DR. SEYMOUR H. SILVERS.

Miss W., aged 19, is presented from Kings County Hospital. Two years ago she noticed the gradual appearance of small pink pimples over the neck and shoulders. These increased in size and number. Many coalesced and changed in color. Later similar areas appeared on the forehead and temples. The lesions over the shoulders frequently became oily and scaly. The lesions are pruritic. The past history is irrelevant, and the patient is otherwise in good health. The patient's mother has had a similar condition of her skin for many years.

Examination shows over the face, neck and upper portion of the shoulders numerous papular pigmented lesions, through each of which a hair is seen to protrude. In some areas the lesions have coalesced to form small tumor-like masses.

The urine was normal. The Wassermann reaction of the blood was negative. The blood count was within normal limits, and chemical examination of the blood also showed normal results. Histologic examination showed keratosis follicularis.

Book Reviews

La maladie de Besnier-Boeck-Schaumann. By L. M. Pautrier, professeur de clinique des maladies cutanées et syphilitiques à la Faculte de Médecine de Strasbourg. Price $2.05, paper. Pp. 344, with 105 illustrations. Paris: Masson & Cie, 1940.

In the preface Pautrier emphasizes the value of considering dermatology from the viewpoint of histophysiology, physiology, biology and general pathology.

Most illustrative of the value of the broader concept is Besnier-Boeck-Schaumann disease, a new reticuloendotheliosis. This disease can successively, simultaneously or separately invade all parts of the organism extending far beyond the limits of dermatology and including all branches of medicine.

The subject matter is divided into three parts. In the first part of Besnier-Boeck-Schaumann disease is discussed, including discussion of lupus pernio of Besnier and Tenneson, the sarcoids or miliary lupoids of Boeck and the benign lymphogranulomatosis of Schaumann. At first the disease was described as simple dermatologic lesions by Besnier, and this description was later amplified by Boeck. It was Jorgen Schaumann who synthesized these lesions with multiple lesions of the lymphatic system and termed the disease "benign lymphogranuloma." Later he considered the disease to have a special predilection for the hemopoietic system and the cause to be tuberculosis of bovine origin.

The second part, on clinical manifestations, includes a detailed description of the disease as it affects the various tissues and organs and the principal syndromes produced thereby, in order. Lesions of the following structures are discussed: cutaneous teguments (nasal, rhinopharyngeal, palatine and buccal membranes); bone; muscles; lymphatic and hemopoietic organs (ganglions, tonsils, spleen and blood); respiratory system (lungs and tracheobronchial ganglions); glandular organs (parotid, sublingual, mammary, testicular and ovarian glands); viscera (heart, liver, kidneys, intestines and pancreas), and nervous system (eyes). In addition, infantile forms of the disease as recently reported are described.

In the third part miscellaneous subjects are discussed, such as pathologic-anatomic synthesis; reactions to tuberculin tests; general phenomena; variable modes of evolution and prognosis; age, sex and geographic distribution; etiology, treatment.

The essential characteristics of Besnier-Boeck-Schaumann disease are: the semiuniversal involvement of the organism, the multiplicity of the clinical manifestations resulting therefrom, its unusually benign and asymptomatic course and its variable evolution. The disease has frequently been mistaken for tuberculosis, especially when it involves the lungs or viscera and is unaccompanied by cutaneous or peripheral ganglionic manifestations. Rarely is it associated with tuberculosis. The pathologic anatomic picture of the disease is constant but not specific—it is at times exactly simulated by tuberculoid leprosy—and reveals it to be a disease of the reticuloendothelial system, unrelated to the lymphogranulomas and with no predilection for the hemopoietic system. Anergy to tuberculin, occurring in two thirds of the persons affected with the disease, is of some value in differentiating tuberculosis but does not indicate that the disease is of tuberculous nature. The cause of the disease remains unknown; virus infection is suggested. Females are more often affected. Treatment is difficult to evaluate, as unexpected spontaneous

resolution may occur. Local cutaneous lesions respond at times to repeated applications of solid carbon dioxide.

This monograph represents the culmination of constant research and study by the author in the subject for the past four years. It is accompanied by an extensive bibliography and is profusely illustrated by excellent clinical photographs, photomicrographs and roentgenograms. The volume is well edited, is free of typographic errors and is printed on paper of the best quality in clear and legible type.

CORRECTION

In the article by Dr. Herbert L. Traenkle entitled "Epithelioma Adenoides Cysticum, Trichoepithelioma and Basal Cell Cancer: Relation Between These Diseases, as Shown by Histologic Studies of Multiple Benign Cystic Epithelioma," in the November issue (ARCH. DERMAT. & SYPH. **42**:822, 1940), the first three illustrations have been incorrectly numbered: Figure 2 should be figure 1; figure 3 should be figure 2, and figure 1 should be figure 3. The legends as numbered in the ARCHIVES are correct.

INDEX TO VOLUME 42

The asterisk (*) preceding the page number indicates an original article in the Archives. Subject entries are made for all articles. Author entries are made for original articles and society transactions. Book Reviews, Editorials, Obituaries and Society Transactions are indexed under these headings in their alphabetical order under the letters B, E, O and S, respectively.

Abnormalities and Deformities: See also under names of diseases, organs and regions, as Atrophy; Nails, abnormalities; Pigmentation; Skin, abnormalities; etc.
hereditary edema of legs (Milroy's disease) associated with other congenital anomalies, *1113
Abramowitz, E. W.: Amyloidosis cutis (localized), 956, 974
Dermatitis medicamentosa (acetylsalicylic acid?); case for diagnosis, 953
Erythema annulare centrifugum, 392
Granuloma annulare or papulonecrotic tuberculid, 386
Keloid or Kaposi's sarcoma, 976
Leukemia of skin (aleukemia), 686
Lichen planus followed by lichen pilaris (vitamin A deficiency?), 165
Psoriasis pustulosa or dermatitis exfoliativa, 291
Scleroderma; sclerodactylia, 173
Abscess: See under names of organs and regions
Acacia, cutaneous reactivity of guinea pigs to gum arabic (acacia), 950
Acanthosis nigricans, 1159
nigricans associated with masculinizing syndrome, 493
Acarus Scabiei: See Scabies
Acetylglycarsenobenzene: See Syphilis
Achromia: See Nevi; Pigmentation, cutaneous
Acid, Acetylsalicylic: See Salicyl Compounds
Barbituric: See Barbital and Barbital Derivatives
Acne aggregata seu conglobata, 730
chlor-acne in railway workers, 144
clinical study in university students, 344
oil acne, 498
pathogenesis of rosacea; review with reference to emotional factors, 347
radiodermatitis with epitheliomas, 677
rosacea-like tuberculid, 496
rosacea; tuberculid with rosacea-like manifestations, 387
unilateral acneform eruption following Bell's palsy, 182
use of vitamin P-P in treatment of seborrhea and acne; preliminary note, 145
vulgaris, nicotinic acid in treatment, *481
vulgaris; review of histologic changes observed in early lesions, *593
vulgaris, treatment by cryotherapy (slush method), *547
vulgaris; tumor of adrenal cortex, with subsequent juvenile acne vulgaris, hirsutism and precocity, 677
Acrodermatitis chronica atrophicans, 966, 1147
chronica atrophicans and lupus erythematosus, differential diagnosis, *773
chronica atrophicans, extensive, in man, 1161
chronica atrophicans; senile elastosis, 1167
Acrodynia, antiacrodynic properties of certain foods, 659
nicotinic acid in treatment, 486
treated with intramuscular injections of vitamin B_1, 486
Acromegaly and cutis verticis gyrata, *1092
Actinodermatitis: See Roentgen Rays
Actinomycosis: See also Mycetoma
of mandible of cow; treatment by roentgen rays, 533
Adenoma, basophilic, of pituitary, 491
sebaceum and tuberous sclerosis, 1150
sudoriferum, 203
Adie's Syndrome: See under Reflex
Adipose Tissue: See Fat
Adolescence, frequency of certain dermatoses in high school girls; report on 4,700 girls, *475
tumor of adrenal cortex, with subsequent juvenile acne vulgaris, hirsutism and precocity, 677
Adrenals, relation to retarded hair growth in underfed albino rats, 948
scleroderma due possibly to adrenal neoplasm, 969
tumor, with subsequent juvenile acne vulgaris, hirsutism and precocity, 677
tumors; acanthosis nigricans associated with masculinizing syndrome, 493
Age, Old: See Old Age
part played by age and female sex hormones in resistance to infection, 948
Agerite alba; occupational leukoderma, *993
occupational leukoderma; preliminary report, 141
Agranulocytosis: See Granulocytopenia
Alexander, L. J.: Mapharsen in treatment of 40 patients following arsphenamine dermatitis, *919
Allergy: See Anaphylaxis and Allergy
Alopecia areata in dog, 537
cicatrisata (pseudopelade of Brocq), 1170
in Irish setter, 532
localized, of eyebrows and lashes (alopecia areata or trichotillomania), 743
of peroneal regions as constitutional sign of neuroarthritic diathesis, 347
Alveolar Process: See Jaws
American Medical Association, Section on Dermatology and Syphilology, program notice, 658
Ammonia and Ammonium Compounds, mobilization of bismuth produced by ammonium chloride, *868
Amyloidosis cutis (localized), 956, 974
localized, of legs, 723
localized, of tongue, pharynx and eyelids, 723
Amyotrophy: See Atrophy, muscular
Anaphylaxis and Allergy: See also under names of various diseases, as Asthma; Eczema; Rhus, poisoning; etc.
comparison of old tuberculin (Koch) and modified tuberculin (Mellon and Beinhauer); cutaneous reactions in persons with hyperergic and with anergic tuberculoderms, *461
contact reactions in atopy; contact reactions to silkworm in atopic subjects, 949
dermatitis herpetiformis or "id," 230
eczema-asthma-hay fever or asthma-prurigo personality, *786
effect of ointment bases on skin; results of patch tests with commonly used ointment bases, *285
experimental and clinical observations with histaminase, *896
local hemorrhagic necrotic skin reactions in man (Shwartzman phenomenon), 484
oral potassium chloride therapy in asthma, hay fever, urticaria and eczema, 486
parenteral use of hypertonic dextrose for relief of pruritus and of serum sickness, *802
personality factor in psychoneurogenous reactions of skin, *780

Anaphylaxis and Allergy—Continued
symposium on allergic dermatoses; allergic drug eruptions, 1125
symposium on allergic dermatoses; allergic occupational dermatosis, 1128
symposium on allergic dermatoses; allergic reactions to plants, 1126
symposium on allergic dermatoses; atopic dermatitis, 1127
symposium on allergic dermatoses; contact-type eczematous dermatitis, 1125
symposium on allergic dermatoses; fungus allergy, 1127
symposium on allergic dermatoses; infantile eczema, 1126
transference of reagins in blood transfusions, 485
Anderson, C. R.: Acanthosis nigricans associated with masculinizing syndrome, 493
Chronic roentgen ray dermatitis of hands, arms and legs, with epithelioma, 488
Keratosis follicularis (Darier) with remission and exacerbation, 492
Lupus erythematosus involving tongue, 497
Sarcoid of Boeck with uveitis and keratitis, 489
Senear-Usher syndrome (pemphigus erythematodes; chronic benign familial pemphigus; herpetiform dermatitis repens of Ayres and Anderson), 489
Anderson, N. P.: Arsenoresistant syphilis, 358
Basophilic adenoma of pituitary, 491
Darier's disease, 362
Lichen planus of lips and mouth, 505
Multiple benign cystic epithelioma, 506
Norwegian scabies, 499
Pachyonychia congenita in mother and daughter, 365
Perifolliculitis capitis abscedens et suffodiens; cutis verticis gyrata; hydradenitis suppurativa, 492
Telangiectasia following infantile eczema, 506
Andrews, G. C.: Branchial cyst, 389
Cavernous hemangioma of eyelid, 701
Cavernous hemangioma of left inner canthus, 701
Cheilitis; case for diagnosis, 970
Naevus pilosus, 701
Panniculitis following lupus erythematosus, 732
Reticulated pigmented poikiloderma of Civatte, 728
Anemia, ulcers of legs in sickle cell anemia, *1015
Angina, Agranulocytic: See Granulocytopenia
Angina Pectoris in hereditary xanthomatosis, 948
Angioma, Ehlers-Danlos syndrome; 2 cases, 742
multiple, 977
naevus unius lateris (angiomatous), 508
Animals, presentation of cases of cutaneous diseases in, 532
symposium on cutaneous diseases; introduction, 530
symposium on cutaneous diseases in animals; roentgen rays in treatment of diseases in animals, 533
Ankle: See also Foot
Charcot's disease of, 171
Antigens and Antibodies: See also under Eczema; Immunity; Lipoids
influence of dermatitis serum on antibody formation, 663
Anus, anogenital ulcerations on embolic base, 951
cancer in harlequin great dane; treatment by roentgen rays, 534
carcinoma in wire-haired fox terrier; treatment by roentgen rays, 533
Aortitis, nonsyphilitic, and serpiginous syphilid, 221
tertiary syphilis; gumma of soft palate, interstitial sclerosis of testicle, asymptomatic cerebrospinal syphilis and aortitis, 373
Aphthae: See Stomatitis
Apparatus: See also Instruments
massive arsenotherapy in early syphilis by continuous intravenous drip method; technic, *245
Aquaphor: See Cholesterol
Argyll Robertson Pupil: See Pupils
Argyria: See Silver, toxicity
Arms, tertiary syphilis (gummas of arm), 682
Arsenic and Arsenic Compounds: See also Arsphenamines; Tryparsamide
arsenic as cause of cancer of mucous membrane; report of case, *641
arsenical keratoses, 191, 214
dermatitis herpetiformis (treated with sulfanilamide); arsenical keratoses, 961
dermatitis medicamentosa; fixed eruption (due to mapharsen), 960
dermatitis medicamentosa (mapharsen), 967
dermatitis medicamentosa (phenobarbital or carbarsone?), 364
effect of thiosulfate on arsenic excretion, *399
effects of neoarsphenamine and mapharsen on formed elements of blood; granulocytopenia following neoarsphenamine therapy in patient who subsequently received mapharsen without untoward reaction, *909
fixed eruption due to mapharsen, 695
mapharsen in treatment of 40 patients following arsphenamine dermatitis, *919
massive arsenotherapy in early syphilis by continuous intravenous drip method; toxicologic manifestations, *248
relapsing early acute arsenical erythema; report of 2 cases, *30
sensitization to arsenical compounds; sensitization to pentavalent arsenical following use of trivalent arsenical, *808
symposium on syphilis; arsenical dermatitis; monorecidive, followed by arsenical dermatitis; syphilitic onychia due to arsenic? 671
Therapy: See under Syphilis
Arsphenamines, acute interstitial myocarditis following administration of, *312
arsphenamine encephalopathy; report of unusual clinical and histologic observations, *814
clinical investigation of arsphenamine exanthems; statistical investigation of arsphenamine exanthems, 663
dermatitis medicamentosa, 380
effect of neoarsphenamine and mapharsen on formed elements of blood; granulocytopenia following neoarsphenamine therapy in patient who subsequently received mapharsen without untoward reaction, *909
mapharsen in treatment of 40 patients following arsphenamine dermatitis, *919
massive arsenotherapy in early syphilis by continuous intravenous drip method; toxicologic manifestations, *248
melanosis after salvarsan [arsphenamine] dermatitis, 951
sensitization to arsenical compounds; sensitization to pentavalent arsenical following use of trivalent arsenical, *808
symposium on syphilis; acute hemorrhagic encephalitis due to neoarsphenamine, with recovery, 665
Therapy: See under Syphilis
Arthritis, pityriasis-rosea-like dermatitis following gold therapy; report of 2 cases, *1105
Asthma: See also Anaphylaxis and Allergy
eczema-asthma-hay fever or asthma-prurigo personality, *786
Astrachan, G. D.: Lupus vulgaris disseminatus; roentgen ray dermatitis; pulmonary tuberculosis, 1171
Atopy: See Anaphylaxis and Allergy
Atrophoderma: See Atrophy
Atrophy: See also Acrodermatitis chronica atrophicans; Poikiloderma vasculare atrophicans; and under names of organs and regions, as Face; Nerves, optic; etc.

Atrophy—Continued
atrophoderma with telangiectasis, 187
early syphilitic macular atrophy, 983
Gowers' case of local panatrophy, 144
macular; case for diagnosis, 193
macular (Schwenninger and Buzzi type), 194
muscular; scleroderma with secondary unilateral muscular atrophy, 385
Avitaminoses: See under Vitamins
Axilla: See also Sweat Glands
moist papules in, *656
Ayres, S., Jr.: Argyria, 493
Carotinemia, 366
Darier's disease, 362
Dermatophytosis resembling contact dermatitis (cement and tar), 361
Oil acne, 498
Pemphigus of eye or fixed eruption, 498
Recurrent herpetiform dermatitis repens, 490

B C G: See under Tuberculosis
Bacillus: See Bacteria
Back, chronic ulcer; tumor of leg (syphilis or dermatitis artefacta), 691
Bacteria: See Staphylococci; Streptococci; Tubercle Bacillus; Viruses; etc.
Bacterid, chronic pyogenic dermatitis of hands and feet with "bacterid" on arms and trunk, 741
Baehr, G.: Massive arsenotherapy in early syphilis by continuous intravenous drip method; preliminary work with neoarsphenamine, *239
Baldness: See Alopecia
Ball, F. I.: Keratosis palmaris et plantaris, 365
Bamberger-Marie's Disease: See Osteoarthropathy
Bancroft, I. R.: Erythema multiforme limited to plantar and palmar surfaces, 363
Keloid and depressed scars subsequent to ecthymatous rupioid syphilids, 503
Lichenoid eruption due to bismuth; case for diagnosis, 356
Naevus linearis of arm; lichen acuminatus of legs, 501
Bandaging, keratoderma blennorrhagicum (treatment with elastoplast), 347
Barbital and Barbital Derivatives, dermatitis medicamentosa (phenobarbital or carbarsone?), 364
keloidal scars at sites of bullae from barbiturate poisoning, 684
Barnett, C. W.: Iodobismitol with saligenin in treatment of neurosyphilis, *46
Barwasser, N. C.: Congenital dyskeratosis and leukokeratosis oris; case for diagnosis, 1132
Keratosis follicularis (Darier), 1131
Basophilia: See under Pituitary Body
Baxt, H.: Effect of thiosulfate on arsenic excretion, *399
Bazin's Disease: See Erythema induratum
Bechet, P. E.: Acne aggregata seu conglobata, 730
Bromoderma with peculiar purpuric lesions, 209
Dermatitis artefacta, 973
Early atypical lupus erythematosus, 211
Epidermolysis bullosa acquisita, 210, 732
Extensive acrodermatitis chronica atrophicans in man, 1161
Hypertrophic lupus erythematosus, 211
Maduromycosis (black grain variety), 697
Monilial paronychia, 168
Parapsoriasis or purpura annularis telangiectodes, 213
Seborrheic dermatitis, parapsoriasis or cutaneous manifestation of endocrine dysfunction, 731
Skin and Cancer Unit of New York Post-Graduate Medical School and Hospital, Columbia University; historical review, *112
Becker, S. W.: Atrophia pilorum, 1133
Atypical lepra, 188
Beetles, dermatitis linearis due to Paederus idae, 349
Beinhauer, L. G.: Experimental and clinical observations with histaminase, *896
Bell's Palsy: See Paralysis, facial
Bellevue Hospital, massive arsenotherapy in early syphilis by continuous intravenous drip method; follow-up observations at Bellevue Hospital, *267
Benedek, T.: Epidermolysis bullosa dystrophica, 190
Benotti, N.: Excretion of bismuth in urine of patients treated with bismuth ethylcamphorate, *1073
Berkovsky, M.: Atrophy of subcutaneous fat due to protamine zinc insulin, 986
Besnier-Boeck's Disease: See Sarcoid
Biopsy: See Cancer
Bismuth and Bismuth Compounds, bismuth line in long bones of newborn infant, 216
changes in long bones of newborn infants following administration of bismuth during pregnancy, 1124
excretion of bismuth in urine of patients treated with bismuth ethylcamphorate, *1073
lichenoid eruption due to bismuth, 356
mobilization of bismuth produced by ammonium chloride, *868
pemphigoid eruption associated with hemorrhagic nephritis following bismuth therapy; report of case, *59
pigmentation of mouth from bismuth, 169
pigmentation of tongue due to bismuth, 223
Therapy: See under names of various diseases, i. e., Syphilis; etc.
vaginal melanosis caused by bismuth therapy and carcinoma of cervix, *23
Bladder, arsenic as cause of cancer of mucous membrane; report of case, *641
Blank, I. H.: Effect of ointment bases on skin; results of patch tests with commonly used ointment bases, *285
Blastomycosis, 702
Blennorrhagia: See Keratosis blennorrhagica
Blepharochalasis: See Eyelids, diseases
Blood, carotene; carotinemia, 366
Diseases: See Leukemia; etc.
effects of neoarsphenamine and mapharsen on formed elements of blood; granulocytopenia following neoarsphenamine therapy in patient who subsequently received mapharsen without untoward reaction, *909
erythrocyte sedimentation rate and cholesterol contents of blood serum in yaws, 664
fats and lipoids; idiopathic familial lipemia, 659
fungistatic power of blood serum, *426
massive arsenotherapy in early syphilis by intravenous drip method; arsenic excretion in urine and concentration in blood, *270
proteins; blood studies in lymphogranuloma venereum, with reference to serum proteins, 947
sclerosing solutions; photographic method for studying their effects on tissue, *86
transfusion; effect produced on newly contracted syphilis by transfusion of blood taken from patients affected with late stages of syphilis, 1125
transfusions, transference of reagins in, 485
vessels in cornea 35 years after interstitial keratitis, 227
vessels; old blood vessel remains of interstitial keratitis, 226
Bloom, D.: Eczema venenatum (perfume), 968
Lupus erythematosus of mucous membranes, 980
Telangiectatic nevus, 977
Bluefarb, S. M.: Early syphilitic lesions mistaken for dermatophytosis, *11
Erythema elevatum diutinum; report of case, *441
Moist papules in axilla, *656

Boeck Sarcoid: See Sarcoid
Bolus, M.: Exfoliative dermatitis (psoriasis), 351
Bones: See also under names of bones
bismuth line in long bones of newborn infant, 216
changes in long bones of newborn infants following administration of bismuth during pregnancy, 1124
Diseases: See Osteomyelitis; etc.
neurosyphilis and late syphilis of skin, mucous membranes and bones, *456

Book Reviews:
Handbook of Skin Diseases; L. H. Warren, 542
Maladie de Besnier-Boeck-Schaumann; L. M. Pautrier, 1173
Malarial Therapy of General Paralysis and Other Conditions; W. H. Kupper, 398
Modern Dermatology and Syphilology; S. W. Becker and M. E. Obermayer, 750
Reports on Medical Progress 1939 as Published in New England Journal of Medicine; compiled and edited by R. N. Nye, 542
Séro-diagnostic de la syphilis: Etudes comparatives de la sensibilité et de la specifici de différentes réactions actuellement employées; T. M. Vogelsang, 992
The Emperor's Itch; R. Friedman, 991

Bordet-Wassermann Reaction: See Syphilis; Wassermann Reaction
Botryomycosis Hominis: See Granuloma pyogenicum
Bourneville-Pringle Disease: See Sclerosis, tuberous
Bowen's Disease: See Cancer, precancer
Brackett, S.: Pathology of schistosome dermatitis, *410
Brain: See also Nervous System; etc.
arsphenamine encephalopathy; report of unusual clinical and histologic observations, *814
Syphilis: See under Syphilis
torulosis involving human cerebrum, 140
Branchial Apparatus, cyst, 389
Brandt, R.: "Bubonulus" in lymphogranuloma venereum, *811
Breast, eczema mammarum symmetricum, 143
neurofibromatosis associated with carcinoma of breast and pregnancy, *337
Brocq's Disease: See Alopecia cicatrisata
Bromide and Bromine, bromoderma with peculiar purpuric lesions, 209
Bromoderma: See Bromide and Bromine
Brown, C. E.: Acute interstitial myocarditis following administration of arsphenamines, *312
Bubo, Venereal: See Chancroid
Bubonulus: See Lymphogranuloma Venereum
Bucky Rays: See Keratosis follicularis
Bursa, scleroderma over right pectoralis muscle, associated with calcification of right subdeltoid bursa, 688
Buschke's Disease: See Scleroderma
Byrne, J. M.: Effect of thiosulfate on arsenic excretion, *399

Calcification, diffuse morpheiform type of scleroderma with calcinosis (Thibierge-Weissenbach syndrome); improvement under prostigmine bromide therapy, 740
Calcinosis: See Calcification
Callaway, J. L.: Erythroplasia of Queyrat, 350
Leukoderma acquisitum centrifugum, 351
Light-sensitive dermatosis, 350
Multiple benign cystic epithelioma, 352
Callus, symmetric callosities of toes and soles, 747
Calomel: See Skin, diseases
Cancer: See also Melanocarcinoma; Sarcoma; Tumors; and under names of organs and regions, as Anus; Breast; Cheek; Cicatrix; Eyelids; Mucous Membrane; Orbit; Penis; Vulva; etc.
collie with inoperable epidermoid carcinoma of paw; treatment by roentgen rays, 533
dachshund with carcinoma at site of incisor tooth; treatment by roentgen rays, 533
evaluation of risk of biopsy in squamous cell carcinoma, 140
precancer; Bowen's disease, 513
precancer; epithelioma (flat basal cell or Bowen's disease), 392
scotty with interdigital cyst (epidermoid carcinoma); treatment by roentgen rays, 533
Skin and Cancer Unit of New York Post-Graduate Medical School and Hospital, Columbia University; historical review, *112
Cañizares, O.: Relapsing early acute arsenical erythema; report of 2 cases, *30
Treatment of chancroid with sulfanilamide, *649
Canker, hoof canker in horse; treatment by roentgen rays, 533
Cannon, A. B.: Arsenical keratoses, 214
Epidermolysis bullosa; clinical and bacteriologic study; report of 4 cases, *884
Pruritus (icterus); carcinoma of gallbladder, 1154
Ulcer of leg, 957
Capillaries: See also Blood vessels
capillary nevus; case for diagnosis, 1152
Carbarsone: See Arsenic and Arsenic Compounds
Carcinoma: See Cancer
Card, J. F.: Iodobismitol with saligenin in treatment of neurosyphilis, *46
Cardiovascular System: See also Blood vessels
prognosis of syphilis with reference to late complications in, 951
Caro, M. R.: Lupus pernio; case for diagnosis, 200
Toxic eruption following injections of sodium morrhuate, 1149
Carotinemia: See Blood, carotene
Caskey, C. R.: Naevus flammeus, 491
Cells: See Tissue
Cellulitis, streptococcic, of elephantiasis nostras type (recurrent), 738
Cement, dermatophytosis resembling contact dermatitis (cement and tar), 361
Cerebrospinal Fluid: See also Spinal Puncture
immunologic investigations, particularly of lysin, in spinal fluid of tabetic patients infected with relapsing fever, 664
Cervix: See under Uterus
Chancre, pyoderma chancriforme faciei, *447
Soft: See Chancroid
symposium on syphilis; arsenical dermatitis; monorecidive, followed by arsenical dermatitis; syphilitic onychia due to arsenic? 671
syphilitic, acquired by newborn infant during delivery, 661
Chancroid, chronic, of vulva, perineum and inguinal regions, 369
treatment with sulfanilamide, *649
Charache, H.: Neurofibromatosis associated with carcinoma of breast and pregnancy, *337
Charcot's Joints: See under Joints; Tabes Dorsalis
Chargin, L.: Massive arsenotherapy in early syphilis by continuous intravenous drip method; toxicologic manifestations, *248
Cheek, circumscribed scleroderma of; case for diagnosis, 1151
dog with sarcoma on inside of cheek; treatment by roentgen rays, 534

Cheek—Continued
lupus vulgaris of, 706
sublingual papilloma (carcinoma?) involving side of cheek of dog; treatment by roentgen rays, 534
Cheilitis: See under Lips
Chemotherapy: See Syphilis
Chilblains, osteoperiostopathia hypertrophians secundaria associated with perniones; 2 cases, 662
Chloronaphthalene, chlor-acne in railway workers, 144
Cholesterol: See also Lipoids
dermatitis due to aquaphor; report of case, *479
in Blood: See under Blood
Chorioretinitis: See Retinochoroiditis
Christian-Weber's Disease: See Panniculitis
Chrysosis: See under Gold and Gold Compounds
Cicatrix, hypertrophic scarring following eczema vaccinatum, 1165
keloid and depressed scars subsequent to ecthymatous rupioid syphilids, 503
keloidal scars at sites of bullae from barbiturate poisoning, 684
squamous cell carcinoma in scar of lupus vulgaris after trauma; case for diagnosis, 735
Ciliary Body: See Uvea
Cinnamon, dermatitis due to oil of cinnamon, 674
Cipollaro, A. C.: Pachyonychia congenita, 703
Civatte's Disease: See under Poikiloderma
Climate, climatic observations concerning lupus erythematosus in central Anatolia, 348
Clitoris, peniform elephantiasis of praeputium clitoridis in lymphogranuloma venereum, *438
Cohen, D.: Pellagra and myxedema, 1140
Cohen, J. A.: Treatment of chancroid with sulfanilamide, *649
Collagen, proposed classification of cutaneous lipoidoses with description of new local lipoid dermatosis: imbibitio lipoidica collageni degenerati cutis, *68
Collins, L. H., Jr.: Pemphigoid eruption associated with hemorrhagic nephritis following bismuth therapy; report of case, *59
Columbia University, Skin and Cancer Unit of New York Post-Graduate Medical School and Hospital; historical review, *112
Combes, F. C.: Amelanotic melanoma, 689
Erythema elevatum diutinum; report of case, *441
Kaposi's sarcoma; case for diagnosis, 175
Localized scleroderma; lingua geographica; hypertrichosis; keratosis pilaris, 184
Lupus erythematosus with involvement of palpebral conjunctiva, 181
Recurrent symmetric herpes simplex of fingers, 179
Unilateral acneform eruption following Bell's palsy, 182
Conant, N. F.: Extensive lichenified eruption caused by Trichophyton rubrum, *614
Congress: See Societies
Conjunctiva, lupus erythematosus with involvement of palpebral conjunctiva, 181
pemphigus limited to mucosa and conjunctiva, 186
pemphigus of mucous membranes; ocular pemphigus (remissive stage), 228
Conrad, A. H., Jr.: Microsporosis of scalp caused by Microsporum fulvum; report of case and description of fungus, *610
Cornbleet, T.: Bowen's disease, 513
Dermatitis herpetiformis or pemphigus, 189
Generalized scleroderma, 1135
Hydroa vacciniforme or folliculitis ulerythematosa reticulata, 1144
Keratosis follicularis (Darier); case for diagnosis, 1131
Cornbleet, T.—Continued
Pellagra and myxedema, 1140
Pemphigus, 516
Pemphigus vulgaris, 515
Pyoderma faciale, 1133
Cornea, blood vessels in cornea 35 years after interstitial keratitis, 227
Inflammation: See Keratitis
old blood vessel remains of interstitial keratitis, 226
Syphilis: See under Keratitis
Corson, E. F.: Leprosy, rheumatic nodules or circumscribed myxedema, 744
Mobilization of bismuth produced by ammonium chloride, *868
Cosmetics: See Lipstick
Costello, M. J.: Aberrant hair on mucous membrane of lower lip, 171
Amelanotic melanoma, 170
Charcot's disease of ankle, 111
Dermatitis herpetiformis treated successfully with sulfapyridine, 161
Erythema ab igne, 392
Fixed eruption due to mapharsen, 695
Lichen planus, severely excoriated, 162
Livedo racemosa type of tertiary syphilis, 973
Localized scleroderma; lingua geographica; hypertrichosis; keratosis pilaris, 184
Lupus erythematosus and lichen planus, 394
Lupus erythematosus with involvement of palpebral conjunctiva, 181
Melanocarcinoma, 162
Melanocarcinoma following treatment of common mole, 162, 690
Necrobiosis lipoidica; case for diagnosis, 394
Parapsoriasis, 177
Parapsoriasis varioliformis, 165
Pigmentation of mouth from bismuth, 169
Recklinghausen's disease associated with eighth nerve deafness, 172
Recurrent symmetric herpes simplex of fingers, 179
Scleroderma due possibly to adrenal neoplasm, 969
Trophic ulcer of nose, 685
Xanthelasma associated with leprosy, 972
Counter, C. E.: Psoriasis, eczema or palmar syphilid, 502
Courville, C. J.: Pityriasis-rosea-like dermatitis following gold therapy; report of 2 cases, *1105
Coutts, W. E.: Peniform elephantiasis of praeputium clitoridis in lymphogranuloma venereum, *438
Creeping Eruption, 538
Cryotherapy: See under Acne
Cullen, G. E.: Vesicant chemical warfare agents, *123
Culture, cultural aspects of dermatologic thought; president's address, *543
Cummer, C. L.: Dermatitis due to oil of cinnamon, 674
Keloidal scars at sites of bullae from barbiturate poisoning, 684
Papulonecrotic tuberculid, 675
Syphilitic dactylitis; case for diagnosis, 680
Tertiary syphilis (gummas of arm), 682
Trophic elbow joint due to syringomyelia or tertiary syphilis with Charcot joint, 682
Tuberculosis of elbow joint or tertiary syphilis of elbow joint, 683
Tuberculosis verrucosa cutis of more than 60 years' duration, 676
Ulcers of legs in sickle cell anemia, *1015
Vitiligo, 676
Cushing's Disease: See under Pituitary Body
Cutis Elastica: See Skin, abnormalities
Verticis Gyrata: See under Scalp
Cysts: See also under names of organs and regions
Branchial: See Branchial Apparatus
Dermoid: See Tumors, dermoid
scotty with interdigital cyst (epidermoid carcinoma); treatment by roentgen rays, 533

Dactylitis: See Fingers and Toes
Dandruff: See Seborrhea
Danlos-Ehlers Syndrome: See Joints; Skin, abnormalities; Tumors
Darier's Disease: See Keratosis follicularis
Darier-Roussy Sarcoid: See Sarcoid
Darling's Disease: See Histoplasmosis
Deafness, Recklinghausen's disease associated with eighth nerve deafness, 172
Decker, D. A.: Multiple pigmented nevi (malignant?), 745
Decker, H. B.: Mobilization of bismuth produced by ammonium chloride, *868
Deficiency Diseases: See Vitamins
Dennie, C. C.: Massive destruction of face, *1040
De Oreo, G.: Chronic chancroid of vulva, perineum and inguinal regions, 369
Depigmentation: See Pigmentation
Dermatitis: See also Acrodermatitis; Eczema; Neurodermatitis; etc.
Acneform: See Acne
Arsphenamine: See Arsphenamines
artefacta, 973
artefacta; chronic ulcer of back; tumor of leg (syphilis or dermatitis artefacta), 691
Atopic: See Eczema; Neurodermatitis
Atrophicans: See Atrophy
chronic discoid and lichenoid exudative dermatosis, 220
chronic pyogenic, of hands and feet with "bacterid" on arms and trunk, 741
contact, due to mango, 345
contact, from opium derivatives with reference to occupational aspects, 345
dermatophytosis resembling contact dermatitis (cement and tar), 361
eczema or chronic exudative lichenoid discoid dermatosis, 954
Eczematous: See Eczema
exfoliativa, 368
exfoliativa; acute interstitial myocarditis following administration of arsphenamines, *312
exfoliativa, due to naphthalene; report of eruption resembling mycosis fungoides, *53
exfoliativa in horse, 535
exfoliativa or psoriasis pustulosa, 391
exfoliativa (psoriasis), 351
exfoliativa, universal, probable lymphoblastoma, 717
exudative chronic discoid and lichenoid dermatitis (Sulzberger and Garbe); treatment of 5 patients, *322; correction, 658
Gangraenosa: See Gangrene
hemangioma or purpuric lichenoid dermatitis, 396
herpetiformis, 371
herpetiformis in child; case for diagnosis, 198
herpetiformis or "id," 230
herpetiformis or pemphigus, 189
herpetiformis treated successfully with sulfapyridine, 161
herpetiformis (treated with sulfanilamide); arsenical keratoses, 961
infectious; case for diagnosis, 1136
linearis due to Paederus idae, 349
Medicamentosa: See under Drugs; and under names of drugs, as Arsenic and Arsenic Compounds; Arsphenamines; Barbital and Barbital Derivatives; Bismuth and Bismuth Compounds; Gold and Gold Compounds; Quinine; Resorcinol and Resorcinol Derivatives; Salicyl Compounds; Silver; Tryparsamide; etc.
Multiformis: See Dermatitis herpetiformis
Occupational: See Industrial Diseases
of ear, 141
pityriasis-rosea-like dermatitis following gold therapy; report of 2 cases, *1105
repens, recurrent herpetiform, 490
repens; Senear-Usher syndrome (pemphigus erythematodes; chronic benign familial pemphigus; herpetiform dermatitis repens of Ayres and Anderson), 489
Rhus: See Rhus, poisoning
Roentgen Ray: See under Roentgen Rays
Schamberg's disease or pigmented purpuric lichenoid dermatitis, 963
Schistosome: See Schistosomiasis
Seborrheic: See Seborrhea
Solar: See Light, toxicity
Venenata: See under Aquaphor; Cinnamon; Cement; Dyes; Gold and Gold Compounds; Naphthalene; Opium; Tar; Wood; etc.
Verrucosa: See Blastomycosis
Dermatofibrosarcoma protuberans, 1140
Dermatologic societies, directory of, 235, 751
Dermatology, cultural aspects of dermatologic thought; president's address, *543
Dermatolysis: See Skin, abnormalities
Dermatomycosis: See Mycosis, cutaneous
Dermatophytosis: See Mycosis, cutaneous; Ringworm
Dermatoses: See Dermatitis; Eczema; Skin, diseases; etc.
Dermoid Cysts: See Tumors, dermoid
Dextrose, Therapy: See Pruritus
Diabetes Mellitus: See also Xanthoma diabeticorum
atrophy of subcutaneous fat due to protamine zinc insulin, 986
lipoidosis or necrobiosis lipoidica diabeticorum, 363
Diathermy: See under names of various diseases
Diathesis, alopecia of peroneal regions as constitutional sign of neuroarthritic diathesis, 347
Dichloroethylsulfide (Mustard Gas): See Gas
Digestive Tract: See also Intestines
experimental investigation on influence of eczematous processes on protein metabolism, 348
Dinitrochlorobenzene: See Nitrochlorobenzene
Directory of dermatologic societies, 235, 751
Dobes, W. L.: Treatment of acne vulgaris by cryotherapy (slush method), *547
Doty, C. A.: Universal exfoliative dermatitis, probable lymphoblastoma, 717
Drill, use on diseased nails, *1123
Driver, J. R.: Lupus vulgaris erythematodes, Leloir; case for diagnosis, 199
Drugs, Eruptions: See also under names of drugs, as Arsenic and Arsenic Compounds; Arsphenamines; Barbital and Barbital Derivatives; Bismuth and Bismuth Compounds; Gold and Gold Compounds; Quinine; Resorcinol and Resorcinol Derivatives; Salicyl Compounds; Silver; Tryparsamide; etc.
eruptions; gangrene or toxic eruption, 1138
eruptions; symposium on allergic dermatoses; allergic drug eruptions, 1125
Ducrey Vaccine: See Chancroid, diagnosis
Duhring's Disease: See Dermatitis herpetiformis
Durand-Nicolas-Favre's Disease: See Lymphogranuloma Venereum
Dyes, eczema venenatum (dye in clothing), 988
effect on yeast fungi, 349
Dyskeratosis: See Keratosis

Ear: See also Deafness
dermatitis of, 141
digitate verruca on inside of ear of dog; treatment by roentgen rays, 534
etiology of auricular appendages, 147
streptococcic infection of, 738
Ebert, M. H.: Acrodermatitis chronica atrophicans, 1147
Argyria, 1147
Infectious dermatitis; case for diagnosis, 1136
Infectious granuloma; case for diagnosis, 1148
Lichen planus linearis, 1139
Parapsoriasis; case for diagnosis, 1145
Psoriasis or pityriasis rubra pilaris, 517
Recklinghausen's disease with demonstration of nerve fibers in tumor, 190
Sarcoidosis, 520
Syphilitic glossitis, 521
Xanthomatosis, 512

Ecthyma contagiosum; human infection with ecthyma contagiosum, virus disorder of sheep; report of 2 cases, *878
Eczema, chronic exudative lichenoid discoid dermatosis, 954
due to quinine, 958
eczema-asthma-hay fever or asthma-prurigo personality, *786
experimental investigation on influence of eczematous processes on protein metabolism, 348
generalized, in English bull terrier, 532
infantile; symposium on allergic dermatoses, 1126
infantile, telangiectasia following, 506
influence of dermatitis serum on antibody formation, 663
mammarum symmetricum, 143
patchy eczema in dogs, 532
psoriasis or palmar syphilid, 502
Seborrheic: See Seborrhea
simulating lymphoblastoma (mycosis fungoides), 203
some problems concerning pathogenesis of allergic eczemas, elucidated by experiments on sensitization with dinitrochlorobenzene, 147
symposium on allergic dermatoses; contact-type eczematous dermatitis, 1125
vaccinatum, hypertrophic scarring following, 1165
venenatum due to lipstick and nail polish, 224
venenatum due to wooden bracelet, 216
venenatum (dye in clothing), 988
venenatum from nail polish, 218
venenatum (perfume), 968
Edema: See also Elephantiasis; and under names of organs, as Extremities; etc.
hereditary, of legs (Milroy's disease) associated with other congenital anomalies, *1113

EDITORIALS:

William Allen Pusey; tribute to great leader, 940

Ehlers-Danlos Syndrome: See Joints; Skin, abnormalities; Tumors
Elastoplast: See Bandaging
Elbow, squamous cell carcinoma in scar of lupus vulgaris after trauma; case for diagnosis, 735
trophic elbow joint due to syringomyelia or tertiary syphilis with Charcot joint, 682
tuberculosis or tertiary syphilis of elbow joint, 683
Electrocoagulation: See under names of various diseases
Electropyrexia: See under Syphilis
Elephantiasis: See also Lymphogranuloma Venereum
nostras, 151
peniform, of praeputium clitoridis in lymphogranuloma venereum, *438
streptococcic cellulitis of elephantiasis nostras type (recurrent), 738
vulvar; esthiomene; form of granuloma inguinale, 483
Eller, J. J.: Lupus vulgaris of nose; multiple pigmented hemorrhagic sarcoma, 211
Multiple recurrent disseminated painful ulcers; case for diagnosis, 696
Recurrent painful ulcerations of lower lip, 206
Scleroderma over right pectoralis muscle, associated with calcification of right subdeltoid bursa, 688
Elliott, J. A.: Keratosis follicularis, 354
Ellis, F. A.: Effect of ultraviolet radiation on roentgen rays; do ultraviolet rays have deleterious effect on roentgen rays when applied to skin? *466
Embolism, anogenital ulcerations on embolic base, 951
embolia cutis medicamentosa, 484
Emmerson, M. A.: Symposium on cutaneous diseases in animals; roentgen rays in treatment of diseases in animals, 533
Emotions, pathogenesis of rosacea; review with reference to emotional factors, 347
Encephalitis, symposium on syphilis; acute hemorrhagic encephalitis due to neoarsphenamine, with recovery, 665
Endocrine Glands: See also Hormones
seborrheic dermatitis, parapsoriasis or cutaneous manifestation of endocrine dysfunction, 731
Engeler, J. E.: Chronic chancroid of vulva, perineum and inguinal regions, 369
Engman, M. F.: Histochemical study of neurodermatitis; preliminary report; microincineration and spectrographic analysis, *109
Environment and skin disease, 1129
Epidermolysis bullosa, 176
bullosa acquisita, 175, 210, 517, 732
bullosa; clinical and bacteriologic study; report of 4 cases, *884
bullosa, congenital cutaneous defects caused by form of, 487
bullosa dystrophica, 190
Epidermophyton: See Fungi
Epithelioma adenoides cysticum, trichoepithelioma and basal cell cancer; relation between these diseases, as shown by histologic studies of multiple benign cystic epithelioma, *822; correction, 1174
chronic roentgen ray dermatitis of hands, arms and legs, with epithelioma, 488
flat basal cell or Bowen's disease, 392
fungating iodide eruption of tongue or squamous cell epithelioma of tongue, 528, 990
granuloma annulare, annular erythema multiforme perstans, erythema elevatum diutinum, intraepidermal epitheliomatosis or porokeratosis of Mibelli, 746
intraepidermal, 736
mixed cell epithelioma arising from hair follicle in boy aged 11 years, 396
multiple benign cystic, 352, 506
pseudoepitheliomatous hyperplasia, *856
squamous cell epithelioma of tongue, 985
therapeutic results in 100 cases of epithelioma of lid treated by irradiation at Radium Institute of Paris between 1935 and 1937, 660
with radiodermatitis, 677
Epstein, N. N.: Effects of neoarsphenamine and mapharsen on formed elements of blood; granulocytopenia following neoarsphenamine therapy in patient who subsequently received mapharsen without untoward reaction, *909
Epstein, S.: Staphylococcic impetigo contagiosa, *840
Tuberculosis of lungs in patients with sarcoidosis, granuloma annulare and lupus erythematosus; comparison, based on roentgenologic statistics, with its incidence in patients with proved tuberculosis of skin and with different stages of syphilis, *1
Epstein, S. S.: Gentian violet in Sabouraud's medium for isolation of pathogenic fungi, *308
Erysipelas, cutaneous lesions of swine erysipelas, 536
fatality rates in treatment of 998 patients; influence of sulfanilamide, 346
Erysipeloid, infection of peacock with Erysipelothrix rhusiopathiae, followed by case of human erysipeloid, 144
Erythema ab igne, 150, 392
annulare centrifugum, 392
annulare centrifugum of Darier; erythema figuratum, 1172
elevatum diutinum; case for diagnosis, 154, 362
elevatum diutinum, granuloma annulare, annular erythema multiforme perstans, intraepidermal epitheliomatosis or porokeratosis of Mibelli, 746
elevatum diutinum; report of case, *441

Erythema—Continued
figuratum (erythema annulare centrifugum of Darier), 1172
figuratum perstans, 724, 1143
induratum, 395
multiforme, case for diagnosis, 1164
multiforme limited to plantar and palmar surfaces, 363
multiforme perstans, annular, granuloma annulare, erythema elevatum diutinum, intraepidermal epitheliomatosis or porokeratosis of Mibelli, 746
multiforme; recurring erythema multiforme associated with pregnancy, 206
of face in monkeys (Macaca suscata), 539
relapsing early acute arsenical erythema; report of 2 cases, *30
Erythrocytes, Sedimentation: See under Blood
Erythroderma, Ichthyosiforme: See Ichthyosis
Erythroplasia: See Penis
Erythrose peribuccale pigmentaire (Brocq), 989
Esthiomene: See Elephantiasis, vulvar
Estrogens: See also Hormones, sex
purpura due to injection of estrogenic substance, *138
severe allergic dermatitis following parenteral use of theelin [estrone], 346
Estrone: See Estrogens
Exanthem of acute mononucleosis, 344
Extremities, Blood Supply: See Raynaud's Syndrome
localized solid edema (myxedema), 1148
Eyebrows, localized alopecia of eyebrows and lashes (alopecia areata or trichotillomania), 743
Eyelashes, localized alopecia of eyebrows and lashes (alopecia areata or trichotillomania), 743
Eyelids, aleukemic lymphosis involving upper lids with pathologic findings, 659
carcinoma of third eyelid extending onto orbit in western horse; treatment by roentgen rays, 533
cavernous hemangioma of, 701
cavernous hemangioma of left inner canthus, 701
diseases; early bilateral blepharochalasis, 504
localized amyloidosis of tongue, pharynx and eyelids, 723
lupus erythematosus with involvement of palpebral conjunctiva, 181
pemphigus limited to mucosa and conjunctiva, 186
therapeutic results in 100 cases of epithelioma treated by irradiation at Radium Institute of Paris between 1935 and 1937, 660
Eyes: See also Orbit; and under names of special structures and diseases of eye, as Retina; etc.
dermoid tumor in dachshund, 532
pemphigus of, or fixed eruption, 498

Face, lichen planus with pigmentation of face, 368
linear scleroderma with facial hemiatrophy, 741
massive destruction of, *1040
Paralysis: See Paralysis, facial
syringocystoma confined to face, 510
Falconer, E. H.: Effects of neoarsphenamine and mapharsen on formed elements of blood; granulocytopenia following neoarsphenamine therapy in patient who subsequently received mapharsen without untoward reaction, *909
Fanburg, S. J.: Dermatitis due to aquaphor; report of case, *479
Exfoliative dermatitis due to naphthalene; report of eruption resembling mycosis fungoides, *53
Fat: See also Lipoids
atrophy of subcutaneous fat due to protamine zinc insulin, 986
in Blood: See Blood, fats and lipoids
sclerema adiposum neonatorum, 487
Favre-Nicolas' Disease: See Lymphogranuloma Venereum
Feces, occurrence of Monilia in normal stools, 659
Feer's Disease: See Acrodynia
Feet: See Foot
Feiler, H. B.: Eczema venenatum due to lipstick and nail polish, 224
Keratosis follicularis (Darier), 222
Tuberculosis of skin; case for diagnosis, 523
Feldbau, E.: Massive arsenotherapy in early syphilis by intravenous drip method; arsenic excretion in urine and concentration in blood, *270
Feldman, S.: Bismuth line in long bones of newborn infant, 216
Fever, Relapsing: See Relapsing Fever
Therapeutic: See under Syphilis; etc.
Fibrosarcoma of shoulder; case for diagnosis, 195
Fibrositis circumscripta or paraffinoma, 233
Fifth Venereal Disease: See Granuloma inguinale
Fingers and Toes: See also Foot; Hand
Nails: See Nails
recurrent symmetric herpes simplex of fingers, 179
symmetric callosities of toes and soles, 747
syphilitic dactylitis; case for diagnosis, 680
Fisher, S.: Sensitization to arsenical compounds; sensitization to pentavalent arsenical following use of trivalent arsenical, *808
Fistula from retained dental root, *938
Folklore: See under Medicine
Folliculitis ulerythematosa reticulata or hydroa vacciniforme, 1144
Foot: See also Fingers and Toes; etc.
superficial noninflammatory lesions of feet, 234
symmetric callosities of toes and soles, 747
treatment of dermatophytosis pedis with medicated insoles, *576
Ford, W. K.: Arsenical keratoses, 191
Macular atrophy; case for diagnosis, 193
Foreign Bodies, unusual case of keratosis suprafollicularis with pili incarnati inciting foreign body reaction, 371
Foreskin: See Penis
Foster, P. D.: Early bilateral blepharochalasis, 504
Rosacea-like tuberculid, 496
Fourth Venereal Disease: See Lymphogranuloma Venereum
Fox, H.: Dermatophytosis of keratotic type; case for diagnosis, 207
Leprosy (mixed type), 1159
William Allen Pusey; tribute to great leader, 940
Frambesia, erythrocyte sedimentation rate and cholesterol contents of blood serum in yaws, 664
Franks, A. G.: Sensitization to arsenical compounds; sensitization to pentavalent arsenical following use of trivalent arsenical, *808
Freeman, H. E.: Tertiary syphilis; gumma of soft palate, interstitial sclerosis of testicle, asymptomatic cerebrospinal syphilis and aortitis, 373
Tumor of adrenal cortex, with subsequent juvenile acne vulgaris, hirsutism and precocity, 677
Frei Reaction: See Lymphogranuloma Venereum
Fritchey, J. A.: Two cases of Ehlers-Danlos syndrome, 742
Fruchtbaum, L. M.: Dermatophytid; case for diagnosis, 157
Lichen planopilaris (Pringle), 156
Fungi: See also Actinomycosis; Blastomycosis; Mycosis; Ringworm; Trichophytosis; etc.
effect of dyes on yeast fungi, 349
gentian violet in Sabouraud's medium for isolation of pathogenic fungi, *308
superficial noninflammatory lesions of feet, 234
symposium on allergic dermatoses; fungus allergy, 1127
Fungicides: See also Ringworm
fungistatic power of blood serum, *426
Furunculosis, multiple, in scotty, 532

Gallbladder, cancer; pruritus (icterus), 1154
Gangrene: See also Raynaud's Syndrome
or toxic eruption, 1138
Gannon, G. P.: Acetylglycarsenobenzene in treatment of syphilis; preliminary report, *1046
Gas, vesicant chemical warfare agents (dichloroethylsulfide [mustard gas]), *123
Gastrointestinal Tract: See Intestines
Gauvain, E. A.: Lymphangioma circumscriptum, simple and cavernous, 149
Multiple idiopathic hemorrhagic sarcoma (Kaposi), 156
Gellis, S.: Moist papules in axilla, *656
Genitals: See also under names of genitals, as Penis; Vagina; etc.
herpes progenitalis as venereal contagion, *933
Gentian Violet in Sabouraud's medium for isolation of pathogenic fungi, *308
ulcerative reaction in treatment of impetigo contagiosa, *1122
Germanin, Therapy: See Lupus erythematosus
Glick, A. W.: Fungistatic power of blood serum, *426
Glicklich, E. A.: Late syphilis with rare orbital gumma; report of case, *559
Glomus Tumors: See under Tumors
Glossitis: See Tongue
Goebel, M. E.: Erythema ab igne, 150
Xanthoma tuberosum multiplex, 152
Goeckerman, W. H.: Arsenic as cause of cancer of mucous membrane; report of case, *641
Gold and Gold Compounds, gold dermatitis and stomatitis, 721
pityriasis-rosea-like dermatitis following gold therapy; report of 2 cases, *1105
Therapy: See under names of diseases
Goldman, L.: Ulcerative reaction from gentian violet in treatment of impetigo contagiosa, *1122
Vesicant chemical warfare agents, *123
Goldmann, B. A.: Acetylglycarsenobenzene in treatment of syphilis; preliminary report, *1046
Goldstein's Disease: See Telangiectasia
Gonadotropic Substances: See Hormones, sex
Granulocytopenia, effect of neoarsphenamine and mapharsen on formed elements of blood; granulocytopenia following neoarsphenamine therapy in patient who subsequently received mapharsen without untoward reaction, *999
Granuloma annulare, 353
annulare, annular erythema multiforme perstans, erythema elevatum diutinum, intraepidermal epithelioma tosis or porokeratosis of Mibelli, 746
annulare, generalized, 219
annulare or papulonecrotic tuberculid, 386
annulare; tuberculosis of lungs in patients with sarcoidosis, granuloma annulare and lupus erythematosus; comparison, based on roentgenologic statistics, with its incidence in patients with proved tuberculosis of skin and with different stages of syphilis, *1
Fungoides: See Mycosis fungoides
Herxheimer reaction, gumma or nonspecific infected granuloma, 736
infectious; case for diagnosis, 1148
Inguinale, 1124. See also Lymphogranuloma Venereum
inguinale; esthiomene; form of granuloma inguinale, 483
inguinale, experimental and clinical, 141
Lymphadenoid: See Lymphocytoma
nonspecific chronic granuloma, hypertrophic lichen planus or lichenificatio gigantea, 737
nonspecific, on dorsum of tongue of dog; treatment by roentgen rays, 534
pyogenicum; case for diagnosis, 505
Venereal: See Granuloma inguinale
Greenbaum, S. S.: Two cases of Ehlers-Danlos syndrome, 742
Greenberg, S.: Experiments in poison ivy sensitivity; effects of specific injections on level of sensitivity to quantitative patch tests and on clinical susceptibility, *290; correction, 542
Groin, chronic chancroid of vulva, perineum and inguinal regions, 369
Gross, E. R.: Flesh-colored paste to camouflage cutaneous lesions, 224
Interstitial keratitis at age of 60, 227
Localized alopecia of eyebrows and lashes (alopecia areata or trichotillomania), 743
Gross, P.: Morphea or lichen sclerosus et atrophicus of Hallopeau, 383
Poikiloderma vasculare atrophicans (Jacobi), 214
Poikilodermatomyositis; case for diagnosis, 215, 377
Gum Arabic: See Acacia
Gummas: See under Arms; Orbit; Palate; Syphilis, tertiary; etc.
Gums, multiple verrucae in mouth and on gums of dog; treatment by roentgen rays, 534
Guy, W. H.: Acetylglycarsenobenzene in treatment of syphilis; preliminary report, *1046

Hair: See also Alopecia
aberrant hair on mucous membrane of lower lip, 171
atrophia pilorum, 1133
epithelioma adenoides cysticum, trichoepithelioma and basal cell cancer; relation between these diseases, as shown by histologic studies of multiple benign cystic epithelioma, *822
excessive; tumor of adrenal cortex, with subsequent juvenile acne vulgaris, hirsutism and precocity, 677
localized alopecia of eyebrows and lashes (alopecia areata or trichotillomania), 743
localized scleroderma; lingua geographica; hypertrichosis; keratosis pilaris, 184
mixed cell epithelioma arising from hair follicle in boy aged 11 years, 396
relation of adrenals to retarded hair growth in underfed albino rats, 948
unusual case of keratosis suprafollicularis with pili incarnati inciting foreign body reaction, 371
Hall, A. F., Jr.: Boeck's miliary lupoid or leprosy, 507
Psoriasis limited to palmar and plantar surfaces, 364
Hallopeau's Disease: See Lichen sclerosis et atrophicus
Hamilton, C. M.: Xeroderma pigmentosum in Negress, *570
Hamilton, T. R.: Massive destruction of face, *1040
Hand: See also Fingers and Toes
syphilis of; neurodermatitis of calf, 965
Hansen's Disease: See Leprosy
Hardy, M.: Atrophy of optic nerve; old interstitial keratitis (malaria therapy), 228
Fibrositis circumscripta or paraffinoma, 233
Haxthausen's Disease: See Keratosis
Hay Fever: See also Anaphylaxis and Allergy
eczema-asthma-hay fever or asthma-prurigo personality, *786
Hemangioma, cavernous, of eyelid, 701
cavernous, of left inner canthus, 701
multiple, 396
multiple (presented for discussion as to further treatment), 735
or purpuric lichenoid dermatitis, 396
Hemiatrophy: See under Face
Hepatitis: See Jaundice
Herpes gestationis, 982
progenitalis as venereal contagion, *933
simplex, 660
simplex, recurrent symmetric, of fingers, 179
zoster, generalized, associated with leukemia, *587
zoster, statistical clinical observations on, 349

Herxheimer Reaction: See Syphilis
Hidradenitis: See under Sweat Glands
Hill, W. R.: Lichen sclerosus et atrophicus, *755
Proposed classification of cutaneous lipoidoses with description of new local lipoid dermatosis: imbibitio lipoidica collageni degenerati cutis, *68
Hirsutism: See Hair, excessive
Histaminase, experimental and clinical observations, *896
Histamine, experimental and clinical observations with histaminase, *896
experiments as chemical mediator for cutaneous pain, 949
Histoplasmosis of Darling, 140
Hitch, J. M.: Granuloma annulare, 353
Seborrheic eczema, familial; case for diagnosis, 355
Verrucous nevus of groin, hands and feet; case for diagnosis, 356
Hodgkin's Disease: See Lymphogranuloma
Holman, H. H.: Acute disseminated lupus erythematosus; its treatment with sulfanilamide and allied products, *1059
Generalized herpes zoster associated with leukemia, *587
Holtzman, I. N.: Pityriasis rubra pilaris, 153
Hopkins, J. G.: Capillary nevus; case for diagnosis, 1152
Chronic ulcer of back; tumor of leg (syphilis or dermatitis artefacta), 691
Poikiliodermatomyositis; case for diagnosis, 377
Hormones: See also Endocrine Glands; Estrogens; Insulin; etc.
sex; part played by age and female sex hormones in resistance to infection, 948
Hospitals, massive arsenotherapy in early syphilis by continuous intravenous drip method; follow-up observations at Bellevue Hospital, *267
massive arsenotherapy in early syphilis by continuous intravenous drip method; follow-up observations at New York Hospital, *264
Skin and Cancer Unit of New York Post-Graduate Medical School and Hospital, Columbia University; historical review, *112
Howles, J. K.: Black hairy tongue; report of 3 cases, *566
Hughes, R. P.: Use of sulfanilamide in dermatology, *33
Hume, E. B.: Leprosy, rheumatic nodules or circumscribed myxedema, 744
Hydrarthrosis, lymphogranuloma inguinale in children with hydrarthrosis of knee joint; 5 cases, 146
Hydroa vacciniforme or follicultis ulerythematosa reticulata, 1144
Hyman, H. T.: Massive arsenotherapy in early syphilis by continuous intravenous drip method; clinical considerations, *253
Hyperergy: See Anaphylaxis and Allergy
Hyperkeratosis: See Ichthyosis; Keratosis
Hypertrichosis: See Hair
Hypophysis: See Pituitary Body
Hypothyroidism: See Myxedema

Ichthyosis, erythroderma ichthyosiforme congénitale, 527, 955
ichthyoid skin in bull dog, 532
Simplex: See Xeroderma
Icterus: See Jaundice
Imbibitio Lipoidica Collageni Degenerati Cutis: See Skin, diseases
Immunity: See also Anaphylaxis and Allergy
local hemorrhagic necrotic skin reactions in man (Shwartzman phenomenon), 484
part played by age and female sex hormones in resistance to infection, 948
Impetigo contagiosa, staphylococcic, *840
contagiosa, ulcerative reaction from gentian violet in treatment of, *1122
Industrial Diseases, chlor-acne in railway workers, 144
contact dermatitis from opium derivatives with reference to occupational aspects, 345
occupational leukoderma, *993
occupational leukoderma; preliminary report, 141
oil acne, 498
symposium on allergic dermatoses; allergic occupational dermatosis, 1128
treatment of occupational dermatitis with vitamins A and D, 146
vesicant chemical warfare agents, *123
Infants, Newborn: See Newborn Infants
Ingraham, N. R.: Streptococcic infection of ears, 738
Inguinal Glands: See Lymph Nodes
Regions: See Groin
Injections: See Blood, transfusion
Insoles, treatment of dermatophytosis pedis with medicated insoles, *576
Instruments: See also Apparatus
use of drill on diseased nails, *1123
Insulin: See also Diabetes Mellitus
atrophy of subcutaneous fat due to protamine zinc insulin, 986
treatment of cutaneous pruritus with insulin, 487
Internal Secretions: See Endocrine Glands
Intestines, parasites; dermatitis medicamentosa (phenobarbital or carbarsone), 364
Iodide: See Iodine and Iodine Compounds
Iodine and Iodine Compounds, action of iodine on diseases of skin as influenced by season and weather, *1083
fungating iodide eruption of tongue or squamous cell epithelioma of tongue, 528, 990
pyoderma or iododerma, 169
Iodobismitol: See Bismuth and Bismuth Compounds; Syphilis
Iododerma: See under Iodine and Iodine Compounds
Iontophoresis: See Scleroderma
Irgang, S.: Lupus erythematosus profundus; report of example with clinical resemblance to Darier-Roussy sarcoid, *97
Isaak, L.: Sclerosing solutions; photographic method for studying their effects on tissue, *86
Itching: See Pruritus
Ivy Poisoning: See Rhus, poisoning

Jacobi-Petges' Disease: See Poikiloderma vasculare atrophicans
Jacobson, H. P.: Adie's syndrome; pseudo Argyll Robertson pupil, 360
Onychomycosis treated with vaccine, 504
Jarisch-Herxheimer Reaction: See under Syphilis
Jaundice, pruritus (icterus); carcinoma of gallbladder, 1154
xanthomatosis, 512
Jaws, actinomycosis of mandible of cow; treatment by roentgen rays, 533
Jekel, L. G.: Unusual serologic reactions during pregnancy; report of case, *137
Jensen, A. K.: Erythema elevatum diutinum; case for diagnosis, 362
Scleroderma treated with mecholyl iontophoresis, 502
Johnson, H. H.: Unusual case of keratosis suprafollicularis with pili incarnati inciting foreign body reaction, 371
Johnson, H. M.: Congenital linear pigmentation of Negroes, 739
Herxheimer reaction, gumma or nonspecific infected granuloma, 736
Multiple hemangioma (presented for discussion as to further treatment), 735
Johnson, L. M.: Dermatitis herpetiformis or "id," 230
Joints, Ehlers-Danlos syndrome, *450, 742
trophic elbow joint due to syringomyelia or tertiary syphilis with Charcot joint, 682
Journals: See Periodicals
Juxta-Articular Nodules: See Nodes

Kahn Test: See under Syphilis
Kala-Azar: See Leishmaniasis
Kampf, M. B.: Herpes gestationis, 982
Kaplan, A. A.: Ehlers-Danlos syndrome, *450
Kaposi's Sarcoma: See Sarcoma
Keil, H.: Treatment of acne vulgaris by cryotherapy (slush method), *547
Keim, H. L.: Early mycosis fungoides, 718
Kelly, R. J.: Lichen sclerosus et atrophicus, 383
Keloid: See also Cicatrix
and depressed scars subsequent to ecthymatous rupioid syphilids, 503
keloidal scars at sites of bullae from barbiturate poisoning, 684
or Kaposi's sarcoma, 976
Kendrick, F. J.: Mycosis fungoides; case for diagnosis, 510
Mycosis fungoides (prefungoid stage), 510
Kennedy, C. B.: Black hairy tongue; report of 3 cases, *566
Keratitis, atrophy of optic nerve; old interstitial keratitis (malaria therapy), 228
corneal examination and slit lamp microscopy in diagnosis of late congenital syphilis, especially in adults, 344
interstitial, at age of 60, 227
interstitial; blood vessels in cornea 35 years after interstitial keratitis, 227
interstitial; malaria therapy, 229
interstitial, old blood vessel remains of, 226
sarcoid of Boeck with uveitis and keratitis, 489
Keratoderma: See Keratosis
Keratosis: See also Ichthyosis
arsenical, 191, 214
arsenical; dermatitis herpetiformis (treated with sulfanilamide), 961
blennorrhagica, pathogenesis of, 347
congenital dyskeratosis and leukokeratosis oris, 1132
dermatophytosis of keratotic type; case for diagnosis, 207
follicularis, 354
follicularis (Darier), 222, 362, 1131, 1172
follicularis (Darier) with remission and exacerbation, 492
follicularis; dyskeratosis of Darier, of exclusive oral localization, 950
follicularis; treatment of Darier's disease with Bucky rays, 348
granuloma annulare, annular erythema multiforme perstans, erythema elevatum diutinum, intraepidermal epitheliomatosis or porokeratosis of Mibelli, 746
keratoderma blennorrhagicum (treatment with elastoplast), 347
palmaris et plantaris, 365
palmaris et plantaris, acquired type, or Haxthausen's disease, 232
pilaris; localized scleroderma; lingua geographica; hypertrichosis, 184
suprafollicularis; unusual case with pili incarnati inciting foreign body reaction, 371
Kerrigan, L.: Lymphosarcoma; case for diagnosis, 197
Kesten, B. M.: Dermatolysis; case for diagnosis, 384
Kile, R. L.: Use of drill on diseased nails, *1123
King, H.: Xeroderma pigmentosum in Negress, *570
Kingsbury, J.: Recurring erythema multiforme associated with pregnancy, 206
Kirby-Smith, H.: Effect of ultraviolet radiation on roentgen rays; do ultraviolet rays have deleterious effect on roentgen rays when applied to skin? *466
Klauder, J. V.: Blood vessels in cornea 35 years after interstitial keratitis, 227
Flesh-colored paste to camouflage cutaneous lesions, 224
Interstitial keratitis (malaria therapy), 229
Nonspecific effect of antisyphilitic treatment in inflammatory ocular lesions (chorioretinitis), 225
Klauder, J. V.—Continued
Old blood vessel remains of interstitial keratitis, 226
Pemphigus of mucous membranes; ocular pemphigus (remissive stage), 228
Symmetric callosities of toes and soles, 747
Symposium on cutaneous diseases in animals; introduction, 530
Symposium on cutaneous diseases in animals; some common cutaneous diseases in domesticated animals with correlation of same diseases in man, 535
Telangiectatic dysplasia of Rendu-Osler-Weber type, with pigmentary changes, 231
Kline Test: See under Syphilis
Knoll, A. F.: Experimental and clinical observations with histaminase, *896
Knowles, F. C.: Cultural aspects of dermatologic thought; president's address, *543
Kositchek, R. J.: Parenteral use of hypertonic dextrose for relief of pruritus and of serum sickness, *802
Kraurosis: See under Vulva
Kulchar, G. V.: Iodobismitol with saligenin in treatment of neurosyphilis, *46

Labia Majora: See Vulva
Labor: See also Pregnancy
syphilitic chancre acquired by newborn infant during delivery, 661
LaRocco, C. G.: Keloidal scars at sites of bullae from barbiturate poisoning, 684
Papulonecrotic tuberculid, 675
Radiodermatitis with epitheliomas, 677
Sulfapyridine dermatitis; report of 2 cases, *341
Syphilitic dactylitis; case for diagnosis, 680
Tertiary syphilis (gummas of arm), 682
Trophic elbow joint due to syringomyelia or tertiary syphilis with Charcot joint, 682
Tuberculosis of elbow joint or tertiary syphilis of elbow joint, 683
Tuberculosis verrucosa cutis of more than 60 years' duration, 676
Ulcers of legs in sickle cell anemia, *1015
Vitiligo, 676
Larva Migrans: See Creeping Eruption
Laughlen Test: See under Syphilis
Laymon, C. W.: Boeck's sarcoid, 397
Micropapular tuberculid, *625
Legs: See also Foot
chronic inflammatory ulcer; treatment with sulfanilamide ointment, 357
chronic ulcer of back; tumor of leg (syphilis or dermatitis artefacta), 691
indolent ulceration of, 152
localized amyloidosis of, 723
ulcer, 957
ulcers in sickle cell anemia, *1015
Leifer, W.: Massive arsenotherapy in early syphilis by continuous intravenous drip method; technic, *245
Leiomyoma cutis, 508
Leishmaniasis, local treatment of ulcerated oriental sore by powder of certain sulfonamide derivatives, 1130
Lentigo in chimpanzees (Pan Satyrus), 539
Lentz, J. W.: Intraepidermal epithelioma, 736
Nonspecific chronic granuloma, hypertrophic lichen planus or lichenificatio gigantea, 737
Symposium on cutaneous diseases in animals; presentation of cases and lantern slides, 532
Leprosy, atypical lepra, 188
mixed type, 1159
or Boeck's miliary lupoid, 507
rheumatic nodules or circumscribed myxedema, 744
with juxta-articular nodes, 1162
xanthelasma associated with, 972
Lerner, M.: Elephantiasis nostras, 151
Leukemia, aleukemic lymphosis involving upper lids with pathologic findings, 659
and leukemid, 214
generalized herpes zoster associated with leukemia, *587

Leukemia—Continued
leukemid, 1156
lymphatic, 687
monocytic, 952
mycosis fungoides, leukemid or Hodgkin's disease of skin, 1157
myelogenous, 195
myelogenous leukaemia cutis, 495
of skin, 1162
of skin (aleukemia), 686
Leukemid: See under Leukemia
Leukocytes: See Leukemia
Leukoderma: See Vitiligo
Leukokeratosis: See Mouth, leukoplakia
Leukoplakia: See Mouth
Levine, B.: Cheilitis exfoliativa, 370
Dermatitis exfoliativa, 368
Dermatitis herpetiformis, 371
Levy, N. A.: Arsphenamine encephalopathy; report of unusual clinical and histologic observations, *814
Lewis, G. M.: Blastomycosis, 702
Cheilitis, 159
Dermatitis herpetiformis (treated with sulfanilamide); arsenical keratoses, 961
Dermatitis medicamentosa; fixed eruption (due to mapharsen), 960
Dermatophytosis (tinea corporis), 962
Eczema (due to quinine?), 958
Epithelioma (flat basal cell or Bowen's disease), 392
Lichen planus of nail bed; report of case, *607
Mycetoma, 160
Pyoderma, 390
Urticaria pigmentosa (adult type), 967
Lice: See Pediculosis
Lichen acuminatus of legs; naevus linearis of arm, 501
moniliformis, case for diagnosis, 167
pilaris; lichen planus followed by lichen pilaris (vitamin A deficiency?), 165
planopilaris (Pringle), 156
planus and lupus erythematosus, 394
planus and lupus erythematosus, differential diagnosis, *773
planus, familial; report of 4 cases of lichen planus in 1 family, with brief review of literature, *653
planus followed by lichen pilaris (vitamin A deficiency?), 165
planus, hypertrophic, nonspecific chronic granuloma or lichenificatio gigantea, 737
planus linearis, 1139
planus of lips and mouth, 505
planus of nail bed; report of case, *607
planus or lupus miliaris disseminatus faciei, 710
planus, pigmentation following, 985
planus, severely excoriated, 162
planus; symposium on syphilis; lichen-planus-like recurrent syphiloderm with severe itching, 670
planus with pigmentation of face, 368
sclerosus et atrophicus, 383, *755
sclerosus et atrophicus of Hallopeau or morphea, 383
spinulosus; psoriasis associated with lichen-spinulosus-like eruption, 734
Lichenification: See Neurodermatitis
Light: See also Ultraviolet Rays; etc.
toxicity; chronic polymorphous eruptions due to light, 662
toxicity; light-sensitive dermatosis, 350
toxicity; photosensitization and melanoderma caused by mercurochrome, 661
Lindsay, H. C. L.: Chronic inflammatory ulcer of leg; treatment with sulfanilamide ointment, 357
Dermatitis medicamentosa (phenobarbital or carbarsone?), 364
Primary cutaneous Hodgkin's disease, 500
Lingua: See Tongue
Lipemia: See Blood, fats and lipoids
Lipids: See Blood, fats and lipoids; Lipoids
Lipoidosis: See Lipoids; Xanthoma
Lipoids: See also Cholesterol; Fat; Phosphorus and Phosphorus Compounds
in Blood: See Blood, fats and lipoids
lipoidosis or necrobiosis lipoidica diabeticorum, 363
necrobiosis lipoidica; case for diagnosis, 375, 394
necrobiosis lipoidica diabeticorum without diabetes, 693
necrobiosis without diabetes, 719
proposed classification of cutaneous lipoidoses with description of new local lipoid dermatosis: imbibitio lipoidica collageni degenerati cutis, *68
Liposarcoma, 202
Lips, aberrant hair on mucous membrane of lower lip, 171
cheilitis, 159, 970, 1161
cheilitis and dermatitis from resorcinol and derivative (sucrets), *138
cheilitis exfoliativa, 370
lichen planus of lips and mouth, 505
recurrent painful ulcerations of lower lip, 206
Lipstick, eczema venenatum due to lipstick and nail polish, 224
Littman, S.: Transverse furrows of nails, *874
Livedo racemosa type of tertiary syphilis, 973
Liver Therapy: See Pemphigus; etc.
Livingood, C.: Chronic pyogenic dermatitis of hands and feet with "bacterid" on arms and trunk, 741
Streptococcic cellulitis of elephantiasis nostras type (recurrent), 738
Locasto, C. B.: Multiple idiopathic hemorrhagic sarcoma (Kaposi), 156
Lofgren, R. C.: Linear scleroderma with facial hemiatrophy, 741
Loftis, E. L.: Purpura due to injection of estrogenic substance, *138
Recklinghausen's disease in identical twins, *657
Long, W. E.: Mapharsen in treatment of 40 patients following arsphenamine dermatitis, *919
Luetin Test: See under Syphilis
Lumbar Puncture: See Spinal Puncture
Lungs, Tuberculosis: See Tuberculosis, pulmonary
Luotest: See under Syphilis
Lupoid: See Sarcoid
Lupus: See also Tuberculosis
erythematosus, 145, 511, 712
erythematosus, acute disseminated; its treatment with sulfanilamide and allied products (promin), *1059
erythematosus and lichen planus, 394
erythematosus; classification and definition of clinical varieties of erythematodes (lupus erythematosus) with reference to its acute and subacute course, 143
erythematosus, climatic observations in central Anatolia, 348
erythematosus, criteria for diagnosis of, 145
erythematosus, differential diagnosis, *774
erythematosus, early atypical, 211
erythematosus, hypertrophic, 211
erythematosus involving tongue, 497
erythematosus of mucous membranes, 980
erythematosus or papulonecrotic tuberculid, 374
erythematosus or poikiloderma, 748
erythematosus, panniculitis following, 732
erythematosus profundus; report of example with clinical resemblance to Darier-Roussy sarcoid, *97
erythematosus, results obtained by inoculating blood into monkeys, 660

Lupus—Continued
erythematosus; results of pulmonary roentgenologic studies of patients with lupus erythematosus, 348
erythematosus, tuberculin reactions in, 348
erythematosus; tuberculosis of lungs in patients with sarcoidosis, granuloma annulare and lupus erythematosus; comparison, based on roentgenologic statistics, with its incidence in patients with proved tuberculosis of skin and with different stages of syphilis, *1
erythematosus with involvement of palpebral conjunctiva, 181
miliaris disseminatus faciei or lichen planus, 710
pernio, case for diagnosis, 200
vulgaris, 201, 707
vulgaris, disseminatus; roentgen ray dermatitis; pulmonary tuberculosis, 1171
vulgaris erythematodes, Leloir; case for diagnosis, 199
vulgaris, extensive, treated by surgical methods, 1152
vulgaris of cheek, 706
vulgaris of nose, 707
vulgaris of nose; multiple pigmented hemorrhagic sarcoma, 211
vulgaris; squamous cell carcinoma in scar of lupus vulgaris after trauma; case for diagnosis, 735
vulgaris successfully treated with injections of starch, 185
Lymph Nodes: See also Lymphogranuloma; Lymphosarcoma
strumous bubo of tuberculous and lymphogranulomatous origin, 146
Lymphadenosis: See Leukemia, lymphatic
Lymphangioma circumscriptum, simple and cavernous, 149
Lymphedema: See Elephantiasis
Lymphoblastoma, 987. See also Lymphogranuloma
eczema simulating lymphoblastoma (mycosis fungoides), 203
in mice following administration of carcinogenic tar, 140
universal exfoliative dermatitis, probable lymphoblastoma, 717
Lymphocytes: See Leukemia, lymphatic
Lymphocytoma, chronic localized inflammation characterized by lymphadenoid structure, 146
Lymphogranuloma: See also Granuloma
Inguinale: See Granuloma inguinale; Lymphogranuloma Venereum
mycosis fungoides, leukemid or Hodgkin's disease of skin, 1157
primary cutaneous Hodgkin's disease, 500
Lymphogranuloma Venereum, blood studies with reference to serum proteins, 947
"bubonulus" in, *811
clinical observations of primary lesion in, 662
lymphogranuloma inguinale in children with hydrarthrosis of knee joint; 5 cases, 146
peniform elephantiasis of praeputium clitoridis in, *438
primary lesion of; second report, 663
question of congenital transmission, 950
strumous bubo of tuberculous and lymphogranulomatous origin, 146
treatment of 300 cases, with reference to use of Frei antigen intravenously, 947
Lymphopathia Venereum: See Lymphogranuloma Venereum
Lymphosarcoma, case for diagnosis, 197
Lynch, F. W.: Acne vulgaris; review of histologic changes observed in early lesions, *593
Nicotinic acid in treatment of acne vulgaris, *481
MacCardle, R. C.: Histochemical study of neurodermatitis; preliminary report; microincineration and spectrographic analysis, *109
McDonald, F.: Lichen planus with pigmentation of face, 368
Machacek, G. F.: Tuberculid with rosacea-like manifestations, 387
MacKee, G. M.: Mikulicz' disease; case for diagnosis, 726
McLaughlin, R. R. M.: Necrobiosis lipoidica; case for diagnosis, 375
Scleroderma with secondary unilateral muscular atrophy, 385
McNamara, D. H.: Acute interstitial myocarditis following administration of arsphenamines, *312
McNitt, C. W.: Dermatitis medicamentosa (arsphenamine), 380
Madden, J. F.: Hemangioma or purpuric lichenoid dermatitis, 396
Juvenile xanthoma, 395
Mixed cell epithelioma arising from hair follicle in boy aged 11 years, 396
Madura Foot: See Mycetoma
Maduromycosis: See Mycetoma
Magnesium, histochemical study of neurodermatitis; preliminary report; microincineration and spectrographic analysis, *109
Mahoney, J. F.: Massive arsenotherapy in early syphilis by continuous intravenous drip method; résumé of serologic observations, *262
Majocchi's Disease: See Purpura annularis telangiectodes
Malaria, Quartan: See under Syphilis
Therapeutic: See Keratitis; Syphilis
Mallozzi, E. D.: Experiments in poison ivy sensitivity; effects of specific injections on level of sensitivity to quantitative patch tests and on clinical susceptibility, *290; correction, 542
Mammary Gland: See Breast
Mange, follicular, in dogs, 532
Mango, contact dermatitis due to, 345
Mann, W.: Massive arsenotherapy in early syphilis by intravenous drip method; arsenic excretion in urine and concentration in blood, *270
Mantoux Test: See under Tuberculosis
Mapharsen: See Arsenic and Arsenic Compounds; Syphilis
Marie-Bamberger's Disease: See Osteoarthropathy
Martin, H. M.: Symposium on cutaneous diseases in animals; parasites affecting skin, 535
Masculinization: See Virilism
Mattice, M. R.: Effect of thiosulfate on arsenic excretion, *399
Maynard, M. T.-R.: Superficial noninflammatory lesions of feet, 234
Mecholyl, Therapy: See Scleroderma
Medicine, dermatology and folklore, 1129
Melanin: See also Melanoma; Pigmentation
melanodermatitis, 990
pigmentation; case of melanosis after salvarsan [arsphenamine] dermatitis, 951
Melanocarcinoma, 162
following treatment of common mole, 162, 690
Melanoderma: See Pigmentation, cutaneous
Melanoma, amelanotic, 170, 689
Melanosis: See Pigmentation, cutaneous
Meningitis, arsphenamine encephalopathy; report of unusual clinical and histologic observations, *814
Menstruation, menstrual cycle and blood serologic test for syphilis, 484
Mercurochrome, photosensitization and melanoderma caused by, 661
Mercurous Chloride, Therapy: See Skin, diseases
Mesquite, dermatitis due to mesquite wood; report of case, *937

Metals: See Silver; etc.
Metasyphilis: See Syphilis, congenital
Mibelli's Disease: See Keratosis
Michelson, H. E.: Erythema induratum, 395
Micropapular tuberculid, *625
Multiple hemangiomas, 396
Pemphigus erythematodes (Senear-Usher), 397
Microfilm copying of original articles, 658
Microincineration: See Skin, chemistry
Microscopy: See under Keratitis
Microsporosis. Microsporon infection in dachshund, 532
of scalp caused by Microsporum fulvum; report of case and description of fungus, *610
Mikulicz' Disease, case for diagnosis, 726
Miller, J. L.: Mycosis fungoides; case for diagnosis, 376
Syphilid of hand; neurodermatitis of calf, 965
Milroy's Disease: See Edema, hereditary
Mintzer, I. J.: Frequency of certain dermatoses in high school girls; report on 4,700 girls, *475
Miskjian, H. G.: Psoriasiform parakeratosis (Brocq), dry type, 372
Xanthoma tuberosum, 367
Mitchell, J. H.: Case for diagnosis, 519
Epidermolysis bullosa acquisita, 517
Molds: See Fungi
Moles: See Nevi
Molluscum contagiosum, 539
Monetta, O.: Pen'form elephantiasis of praeputium clitoridis in lymphogranuloma venereum. *438
Monilia, monilial paronychia, 168
occurrence in normal stools, 659
Monocytes: See Leukemia, monocytic
Mononucleosis, acute, exanthem of, 344
Montgomery, A. H.: Acrodermatitis chronica atrophicans, 966
Montgomery, D. W.: Injuries of mouth caused by teeth, *333
Montgomery, H.: Lichen sclerosus et atrophicus, *755
Moore, M.: Microsporosis of scalp caused by Microsporum fulvum; report of case and description of fungus, *610
Morphea: See Scleroderma
Mosely, V.: Sarcoid, 352
Mouth: See also Gums; Stomatitis; etc.
dyskeratosis of Darier, of exclusive oral localization, 950
injuries caused by teeth, *333
leukoplakia; congenital dyskeratosis and leukokeratosis oris, 1132
lichen planus of lips and mouth, 505
multiple verrucae in mouth and on gums of dog; treatment by roentgen rays, 534
periadenitis mucosa necrotica recurrens (Sutton); ulcus neuroticum mucosa oris (Loblowitz), 144
pigmentation from bismuth, 169
Mucous Membrane: See also Lips; Mouth; etc.
arsenic as cause of cancer of mucous membrane; report of case, *641
lupus erythematosus of, 980
neurosyphilis and late syphilis of skin, mucous membranes and bones, *456
pemphigus limited to mucosa and conjunctiva, 186
primary tuberculous infection of skin and mucous membrane, 147
Muscles, scleroderma over right pectoralis muscle, associated with calcification of right subdeltoid bursa, 688
Mustard Gas: See under Gas
Mycetoma, 160
maduromycosis (black grain variety), 697
Mycobacterium Leprae: See under Leprosy
Mycosis: See also Actinomycosis; Blastomycosis; Mycetoma; Nails; Ringworm; Stomatitis; Tinea; Trichophytosis; etc.
cutaneous; dermatophytid; case for diagnosis, 157
cutaneous; dermatophytosis of keratotic type; case for diagnosis, 207
cutaneous; dermatophytosis resembling contact dermatitis (cement and tar), 361
cutaneous; dermatophytosis (tinea corporis), 962
cutaneous; maduromycosis (black grain variety), 697
cutaneous; treatment of dermatophytosis pedis with medicated insoles, *576
fungoides; case for diagnosis, 376, 510, 1162
fungoides, early, 718
fungoides; eczema simulating lymphoblastoma, 203
fungoides; exfoliative dermatitis due to naphthalene; report of eruption resembling mycosis fungoides, *53
fungoides, leukemid or Hodgkin's disease of skin, 1157
fungoides or reticuloendotheliosis, 699
fungoides (prefungoid stage), 510
Myelosis, Aleukemic: See Leukemia, myelogenous
Myocarditis, acute interstitial, following administration of arsphenamines, *312
Myositis, poikilodermatomyositis, 215, 377
Myxedema and pellagra, 1140
and xanthoma tuberosum; report of case, *419
circumscribed, leprosy or rheumatic nodules, 744
localized solid edema of extremities (myxedema), 1148

Nails: See also Paronychia
abnormalities; pachyonychia congenita in mother and daughter, 365
discoloration due to nail enamel, *480
eczema venenatum due to lipstick and nail polish, 224
eczema venenatum from nail polish, 218
lichen planus of nail bed; report of case, *607
onychomycosis treated with vaccine, 504
pachyonychia congenita, 703
symposium on syphilis; arsenical dermatitis; monorecidive, followed by arsenical dermatitis; syphilitic onychia due to arsenic? 671
transverse furrows of, *874
use of drill on diseased nails, *1123
Naphthalene, exfoliative dermatitis due to; report of eruption resembling mycosis fungoides, *53
Nares: See Nose
Necrobiosis lipoidica, case for diagnosis, 375, 394
lipoidica diabeticorum or lipoidosis, 363
lipoidica diabeticorum without diabetes, 693
without diabetes, 719
Negroes, xeroderma pigmentosum in Negress, *570
Neoarsphenamine: See Arsphenamines; Syphilis
Neoplasms: See Cancer; Sarcoma; Tumors
Nephritis, pemphigoid eruption associated with hemorrhagic nephritis following bismuth therapy; report of case, *59
Nerves: See also Neuritis; Paralysis
optic, atrophy of; old interstitial keratitis (malaria therapy), 228
optic; pathology and pathogenesis of syphilitic primary optic atrophy, 484
Recklinghausen's disease associated with eighth nerve deafness, 172
Recklinghausen's disease with demonstration of nerve fibers in tumor, 190
Nervous System: See also Brain; Nerves; Reflex; etc.
alopecia of peroneal regions as constitutional sign of neuroarthritic diathesis, 347
diseases; case for diagnosis, 519
Syphilis: See Syphilis

Neuhauser, I.: Gangrene or toxic eruption, 1138
Kaposi's sarcoma, 514
Lupus erythematosus, 511
Macular atrophy (Schwenninger and Buzzi type), 194
Neurocutaneous Syndrome: See under Skin
Neurodermatitis, histochemical study; preliminary report; microincineration and spectrographic analysis, *109
nodular circumscribed giant lichenification of scrotum, 145
nonspecific chronic granuloma, hypertrophic lichen planus or lichenificatio gigantea, 737
of calf; syphilis of hand, 965
symposium on allergic dermatoses; atopic dermatitis, 1127
Neurofibromatosis associated with carcinoma of breast and pregnancy, *337
Recklinghausen's disease associated with eighth nerve deafness, 172
Recklinghausen's disease in identical twins, *657
Recklinghausen's disease with demonstration of nerve fibers in tumor, 190
Neuroses and Psychoneuroses, personality factor in psychoneurogenous reactions of skin, *780
psychoneurogenous component of cutaneous reaction mechanisms, 947
Neurosyphilis: See Syphilis
Nevi: See also Angioma
capillary nevus; case for diagnosis, 1152
melanocarcinoma following treatment of common mole, 162, 690
multiple pigmented, 720
multiple pigmented (malignant?), 745
naevus cerebriformis (cerebelliformis) of scalp, 704
naevus flammeus, 491
naevus linearis of arm; lichen acuminatus of legs, 501
naevus pilosus, 701
naevus unius lateris (angiomatous), 508
telangiectatic, 977
turban tumors; report of case with unusual pathologic findings, including both epidermal and dermal nevi, *15
verrucous, of groin, hands and feet; case for diagnosis, 356
New York Hospital, massive arsenotherapy in early syphilis by continuous intravenous drip method; follow-up observations at New York Hospital, *264
New York Post-Graduate Medical School and Hospital, Columbia University, Skin and Cancer Unit; historical review, *112
Newborn Infants, bismuth line in long bones of, 216
changes in long bones following administration of bismuth during pregnancy, 1124
studies on secretion of sweat in, 663
Newman, B. A.: Adie's syndrome; pseudo Argyll Robertson pupil, 360
Nicolas-Favre Disease: See Lymphogranuloma Venereum
Niles, H. D.: Eczema or chronic exudative lichenoid discoid dermatosis, 954
Scleroderma (progressive type), 183
Nipples: See Breast
Nisbet, T. W.: Granuloma pyogenicum; case for diagnosis, 505
Pyoderma faciale (O'Leary), 503
Nitrochlorobenzene, cutaneous sensitization studies; gross and microscopic changes in ragweed and 2-4 dinitrochlorobenzene sensitization of guinea pigs, and in poison ivy sensitizations of human beings, 142
some problems concerning pathogenesis of allergic eczemas, elucidated by experiments on sensitization with dinitrochlorobenzene, 147
Nodes: See also Panniculitis; etc.
juxta-articular; syphilis, 515
leprosy with juxta-articular nodes, 1162
Nomland, R.: Human infection with ecthyma contagiosum, virus disorder of sheep; report of 2 cases, *878
Nose, gangrene or toxic eruption, 1138
lupus vulgaris of, 707
lupus vulgaris of; multiple pigmented hemorrhagic sarcoma, 211
trophic ulcer of, 685

Obermayer, M. E.: Atrophia pilorum, 1133
Atypical lepra, 188
OBITUARIES:
Oulmann, Ludwig, 944
Pusey, William Allen, 542, 940
Occupational Diseases: See Industrial Diseases
Oil acne, 498
dermatitis due to oil of cinnamon, 674
Ointments: See also Cholesterol; Rhus, poisoning; Skin, diseases
dermatitis due to aquaphor; report of case, *479
effect of ointment bases on skin; results of patch tests with commonly used ointment bases, *285
Old Age, interstitial keratitis at age of 60, 227
senile elastosis; acrodermatitis chronica atrophicans, 1167
Oliver, E. A.: Fibrosarcoma of shoulder; case for diagnosis, 195
Lymphosarcoma; case for diagnosis, 197
Occupational leukoderma, *993
Verruca plantaris, *302
Omens, D. V.: Argyria, 1147
Avitaminosis, 193
Dermatofibrosarcoma protuberans, 1140
Erythema figuratum perstans, 1143
Lupus vulgaris, 201
Pityriasis rubra pilaris, 513
Psoriasis with pustular exacerbation, 1136
Syphilitic glossitis, 521
Onychia: See Nails
Onychomycosis: See Nails
Opium, contact dermatitis from opium derivatives with reference to occupational aspects, 345
Orbit, carcinoma of third eyelid extending onto orbit in western horse; treatment by roentgen rays, 533
late syphilis with rare orbital gumma; report of case, *559
Oriental Sore: See Leishmaniasis
Ormsby, O. S.: Atrophoderma with telangiectasia, 187
Lupus vulgaris successfully treated with injections of starch, 185
Pseudoxanthoma elasticum, 508
Tuberculosis verrucosa cutis, 1141
Osler's Disease: See Telangiectasia
Osteoarthopathy, osteoperiostopathia hypertrophians secundaria associated with perniones; 2 cases, 662
Osteomyelitis, early syphilitic osteomyelitis with report of 2 cases, 483

Pace, E. R.: Naevus unius lateris (angiomatous), 508
Pachyonychia: See under Nails
Paederus: See Beetles
Pain, experiments on histamine as chemical mediator for cutaneous pain, 949
Palate, tertiary syphilis; gumma of soft palate, interstitial sclerosis of testicle, asymptomatic cerebrospinal syphilis and aortitis, 373
Panniculitis following lupus erythematosus, 732
Papilloma, sublingual (carcinoma?) involving side of cheek of dog; treatment by roentgen rays, 534
Paraffinoma or fibrositis circumscripta, 233
Parakeratosis: See Parapsoriasis

Paralysis, Bell's: See Paralysis, facial
facial; unilateral acneform eruption following Bell's palsy, 182
symposium on syphilis; bilateral paralysis of abducens nerve following lumbar puncture, 667
Parapsoriasis, 177, 393, 1145
or purpura annularis telangiectodes, 213
psoriasiform parakeratosis (Brocq), dry type, 372
seborrheic dermatitis or cutaneous manifestation of endocrine dysfunction, 731
varioliformis, 165
Parasites, symposium on cutaneous diseases in animals; parasites affecting skin, 535
Parathyroidectomy and scleroderma in bands, 486
Parkhurst, H. J.: Pruritic melanoderma of undetermined origin; case for diagnosis, 725
Paronychia, monilial, 168
Parounagian, M. E.: Multiple angioma, 977
Parrot's Disease: See Pseudoparalysis
Pascher, F.: Exudative chronic discoid and lichenoid dermatitis (Sulzberger and Garbe); treatment of 5 patients, *322; correction, 658
Paste, flesh-colored paste to camouflage cutaneous lesions, 224
Patch Test: See Anaphylaxis and Allergy
Peacock, infection of peacock with Erysipelothrix rhusiopathiae, followed by case of human erysipeloid, 144
Peck, S. M.: Fungistatic power of blood serum, *426
Pediculosis in monkeys, 538
Pellagra: See also Vitamins, B
and myxedema, 1140
Pemphigus, 516, 700
erythematodes (Senear-Usher syndrome), 397, 713
erythematodes; Senear-Usher syndrome (pemphigus erythematodes; chronic benign familial pemphigus; herpetiform dermatitis repens of Ayres and Anderson), 489
limited to mucosa and conjunctiva, 186
of eye or fixed eruption, 498
of mucous membranes; ocular pemphigus (remissive stage), 228
or dermatitis herpetiformis, 189
pemphigoid eruption associated with hemorrhagic nephritis following bismuth therapy; report of case, *59
vulgaris, 515, 715
Penis, erythroplasia of, 673
erythroplasia of Queyrat, 350, 981
psoriasiform carcinoma of, 1129
Perfume, eczema venenatum, 968
Perifolliculitis capitis abscedens et suffodiens; cutis verticis gyrata; hydradenitis suppurativa, 492
Perineum, chronic chancroid of vulva, perineum and inguinal regions, 369
Periodicals, microfilm copying, 658
Peristein, M.: Adenoma sebaceum and tuberous sclerosis, 1150
Perniosis: See Chilblains
Persky, A. M.: Phenolphthalein eruption, 149
Personality factor in psychoneurogenous reactions of skin, *780
Perspiration: See under Sweat Glands
Petges-Jacobi's Disease: See Poikiloderma vasculare atrophicans
Petrolatum, effect of ointment bases on skin; results of patch tests with commonly used ointment bases, *285
Phalanges: See Fingers and Toes
Pharynx, localized amyloidosis of tongue, pharynx and eyelids, 723
Phenobarbital: See Barbital and Barbital Derivatives
Phenolphthalein and Phenolphthalein Derivatives, eruption, 149
Photodermatosis: See Light, toxicity
Photography, colored motion pictures of some common cutaneous diseases in domesticated animals with correlation of same diseases in man, 535
sclerosing solutions; photographic method for studying their effects on tissue, *86
Photosensitization: See Light; Ultraviolet Rays
Pigmentation: See also Melanin; Nevi; Schamberg's Disease; Silver, toxicity; Xeroderma pigmentosum; etc.
congenital linear pigmentation of Negroes, 739
cutaneous; photosensitization and melanoderma caused by mercurochrome, 661
cutaneous; pruritic melanoderma of undetermined origin; case for diagnosis, 725
cutaneous; vaginal melanosis caused by bismuth therapy and carcinoma of cervix, *23
diffuse; incontinentia pigmentii, 148
following lichen planus, 985
lichen planus with pigmentation of face, 368
of mouth from bismuth, 169
of tongue due to bismuth, 223
telangiectatic dysplasia of Rendu-Osler-Weber type, with pigmentary changes, 231
Pili Incarnati: See under Hair
Pillsbury, D. M.: Chronic pyogenic dermatitis of hands and feet with "bacterid" on arms and trunk, 741
Congenital linear pigmentation of Negroes, 739
Psoriasis associated with lichen-spinulosus-like eruption, 734
Squamous cell carcinoma in scar of lupus vulgaris after trauma; case for diagnosis, 735
Streptococcic cellulitis of elephantiasis nostras type (recurrent), 738
Pines, C.: Generalized granuloma annulare, 219
Pigmentation following lichen planus, 985
Pigmentation of tongue due to bismuth, 223
Pinta, White: See Vitiligo
Pituitary Body, basophilic adenoma of, 491
Pityriasis; pityriasis-rosea-like dermatitis following gold therapy; report of 2 cases, *1105
rubra pilaris, 153, 513
rubra pilaris and lupus erythematosus, differential diagnosis, *774
rubra pilaris or psoriasis, 517
Plants, symposium on allergic dermatoses; allergic reactions to plants, 1126
Poikiloderma or lupus erythematosus, 748
poikilodermatomyositis, 215, 377
reticulated pigmented poikiloderma of Civatte, 728
vasculare atrophicans (Jacobi), 214
Poison Ivy: See Rhus, poisoning
Poisons and Poisoning: See Dyes; and under names of substances
Polish, discoloration of nails due to nail enamel, *480
eczema venenatum due to lipstick and nail polish, 224
eczema venenatum from nail polish, 218
Pollen: See Asthma; Hay Fever; Ragweed
Porokeratosis: See Keratosis
Potassium Chloride: See Anaphylaxis and Allergy
Precocity: See under Adolescence
Pregnancy: See also Labor
changes in long bones of newborn infants following administration of bismuth during pregnancy, 1124
herpes gestationis, 982
neurofibromatosis associated with carcinoma of breast and pregnancy, *337
recurring erythema multiforme associated with pregnancy, 256
unusual serologic reactions during, *137
Prepuce: See Penis
Price, G. F.: Tuberculosis of skin, 158
Pringle-Bourneville's Disease: See Sclerosis, tuberous
Promin: See under Lupus erythematosus
Prostigmine: See Calcification; Scleroderma

Protein metabolism, experimental investigation on influence of eczematous processes on, 348
Prurigo, eczema-asthma-hay fever or asthma-prurigo personality, *786
Pruritus, cutaneous, treatment with insulin, 487
icterus; carcinoma of gallbladder, 1154
parenteral use of hypertonic dextrose for relief of pruritus and of serum sickness, *802
pruritic melanoderma of undetermined origin; case for diagnosis, 725
symposium on syphilis; lichen-planus-like recurrent syphiloderm with severe itching, 670
Pseudoepithelioma: See Epithelioma
Pseudoparalysis, Parrot's, in pair of twins of same sex, 950
Pseudopelade: See Alopecia cicatrisata
Pseudoxanthoma elasticum, 508, 680
elasticum with angioid streaks of retina, 155, 1167
Psoriasis associated with lichen-spinulosus-like eruption, 734
eczema or palmar syphilid, 502
exfoliative dermatitis, 351
limited to palmar and plantar surfaces, 364
or pityriasis rubra pilaris, 517
or syphilid, 978
or syphilis, 980
psoriasiform carcinoma of penis, 1129
psoriasiform parakeratosis (Brocq), dry type, 372
pustulosa or dermatitis exfoliativa, 391
vulgaris, dietetic treatment, 662
with pustular exacerbation, 1136
Psychoneuroses: See Neuroses and Psychoneuroses
Puberty: See Adolescence
Public Health, massive arsenotherapy in early syphilis by continuous intravenous drip method; public health aspects, *283
Pupils, Adie's syndrome; pseudo Argyll Robertson pupil, 360
Purpura annularis telangiectodes or parapsoriasis, 213
bromoderma with peculiar purpuric lesions, 209
due to injection of estrogenic substance, *138
haemorrhagica resulting from sedormid, 141
Schamberg's disease or pigmented purpuric lichenoid dermatitis, 963
Pusey, William Allen; tribute to great leader, 940
Pyoderma, 390
chancriforme faciei, *447
faciale, 1133
faciale (O'Leary), 503
or iododerma, 169

Quinine, eczema due to, 958
embolia cutis medicamentosa, 484
Quinn, H. F.: Massive destruction of face, *1040

Radiations: See Roentgen Rays; Ultraviolet Rays; etc.
Radiodermatitis: See under Roentgen Rays
Radium, Therapy: See under names of various diseases
Ragweed, cutaneous sensitization studies; gross and microscopic changes in ragweed and 2-4 dinitrochlorobenzene sensitization of guinea pigs, and in poison ivy sensitizations of human beings, 142
Railroads, chlor-acne in railway workers, 144
Rankin, J. L., Jr.: Epidermolysis bullosa; clinical and bacteriologic study; report of 4 cases, *884
Ranquist, R. C.: Lupus vulgaris successfully treated with injections of starch, 185
Rattner, H.: Dermatitis herpetiformis or pemphigus, 189
Gangrene or toxic eruption, 1138
Generalized scleroderma, 1135
Kaposi's sarcoma, 514
Lupus erythematosus, 511
Pemphigus, 516
Rattner, H.—Continued
Pemphigus vulgaris, 515
Pyoderma faciale, 1133
Ray, L. F.: Effect of ointment bases on skin; results of patch tests with commonly used ointment bases, *285
Raynaud's Syndrome, early; case for diagnosis, 222
Reagins: See Anaphylaxis and Allergy
von Recklinghausen's Disease: See Neurofibromatosis
Reflex, Adie's syndrome; pseudo Argyll Robertson pupil, 360
Relapsing Fever, immunologic investigations, particularly of lysin, in spinal fluid of tabetic patients infected with relapsing fever, 664
Rendu-Osler's Disease: See Telangiectasia
Resorcinol and Resorcinol Derivatives, cheilitis and dermatitis from resorcinol and derivative (sucrets), *138
Reticuloendothelial System: See also Jaundice; Mononucleosis; etc.
reticuloendotheliosis, 748
reticuloendotheliosis; mycosis fungoides (?), 699
Reticuloendotheliosis: See under Reticuloendothelial System
Reticulosis: See under Reticuloendothelial System
Retina, pseudoxanthoma elasticum with angioid streaks of, 155, 1167
Retinochoroiditis, nonspecific effect of antisyphilitic treatment in inflammatory ocular lesions (chorioretinitis), 225
Rheumatism, leprosy, rheumatic nodules or circumscribed myxedema, 744
Rhus, poisoning; cutaneous sensitization studies; gross and microscopic changes in ragweed and 2-4 dinitrochlorobenzene sensitization of guinea pigs, and in poison ivy sensitizations of human beings, 142
poisoning; experiments in poison ivy sensitivity; effects of specific injections on level of sensitivity to quantitative patch tests and on clinical susceptibility, *290; correction, 542
poisoning; nature of excitant of poison ivy dermatitis, *405
poisoning; prophylaxis and treatment of poison ivy dermatitis with extract of Rhus toxicodendron, 485
Riboflavin: See Vitamins, B
Ricchiuti, J. F.: Lichen planus of nail bed; report of case, *607
Rice, J. L.: Massive arsenotherapy in early syphilis by continuous intravenous drip method; public health aspects, *283
Ringworm: See also Mycosis, cutaneous; Tinea; Trichophytosis; etc.
early syphilitic lesions mistaken for dermatophytosis, *11
gentian violet in Sabouraud's medium for isolation of pathogenic fungi, *308
in chimpanzees (Pan Satyrus) and gorilla (Gorilla gorilla), 538
in fox terrier, 532
Riordan, T. J.: Epidermolysis bullosa, 176
Ritchie, E. B.: Congenital dyskeratosis and leukokeratosis oris; case for diagnosis, 1132
Keratosis follicularis (Darier), 1131
Ritter's Disease: See Dermatitis, exfoliativa
Robinson, S. S.: Leiomyoma cutis, 508
Roentgen Rays, chronic roentgen ray dermatitis of hands, arms and legs, with epithelioma, 488
effect of ultraviolet radiation on roentgen rays; do ultraviolet rays have deleterious effect on roentgen rays when applied to skin? *466
lupus vulgaris disseminatus; roentgen ray dermatitis; pulmonary tuberculosis, 1171
radiodermatitis with epitheliomas, 677
Therapy: See under names of organs, regions and diseases, as Actinomycosis; Anus, cancer; Cancer; Verruca; etc.

Rogers, J. D.: Recurrent herpetiform dermatitis repens, 490
Rosen, I.: Chronic ulceration of tongue; case for diagnosis, 979
Erythroplasia of Queyrat, 981
Syphilid or psoriasis, 978
Syphilis or psoriasis, 980
Rosenbach's Disease: See Erysipeloid
Rosenberg, W. A.: Hereditary edema of legs (Milroy's disease) associated with other congenital anomalies, *1113
Rosenfeld, H.: Fungistatic power of blood serum, *426
Rosenthal, T.: Squamous cell epithelioma of tongue, 985
Rostenberg, A.: Erythroderma ichthyosiforme congénitale, 527, 955
Lymphoblastoma; case for diagnosis, 987
Roussy-Darier Sarcoid: See Sarcoid
Rubber, occupational leukoderma, *993
occupational leukoderma; preliminary report, 141

Sachs, P. M.: Turban tumors; report of case with unusual pathologic findings, including both epidermal and dermal nevi, *15
Sachs, W.: Lichen moniliformis; case for diagnosis, 167
Mycetoma, 160
Turban tumors; report of case with unusual pathologic findings, including both epidermal and dermal nevi, *15
Urticaria pigmentosa (bullous type), 975
Saffron, M. H.: Familial lichen planus; report of 4 cases of lichen planus in 1 family, with brief review of literature, *653
Salicyl Compounds, dermatitis medicamentosa (acetylsalicylic acid), 953
Saligenin: See Syphilis
Salvarsan: See Arsphenamines
Samitz, H. A.: Granuloma annulare, annular erythema multiforme perstans, erythema elevatum diutinum, intraepidermal epitheliomatosis or porokeratosis of Mibelli, 746
Sanders, M.: Epidermolysis bullosa; clinical and bacteriologic study; report of 4 cases, *884
Sarcoid, 352, 708
Besnier-Boeck disease, 487
Boeck's, 397
Boeck's miliary lupoid or leprosy, 507
comparison of old tuberculin (Koch) and modified tuberculin (Mellon and Beinhauer); cutaneous reactions in persons with hyperergic and with anergic tuberculoderms, *461
lupus erythematosus profundus; report of example with clinical resemblance to Darier-Roussy sarcoid, *97
of Boeck with uveitis and keratitis, 489
sarcoidosis, 520, 522
tuberculosis of lungs in patients with sarcoidosis, granuloma annulare and lupus erythematosus; comparison, based on roentgenologic statistics, with its incidence in patients with proved tuberculosis of skin and with different stages of syphilis, *1
type of tuberculosis in American Negro, with splenomegaly, 747
Sarcoma: See also Cancer; Tumors; and under names of tumors, as Fibrosarcoma; Liposarcoma; Lymphosarcoma; etc.
dog with sarcoma on inside of cheek; treatment by roentgen rays, 534
in axillary region of beagle; treatment by roentgen rays, 534
in dog, 537
Kaposi's, 174, 175, 192, 514
Kaposi's, or keloid, 976
lupus vulgaris of nose; multiple pigmented hemorrhagic sarcoma, 211
multiple idiopathic hemorrhagic (Kaposi), 156
Sayer, A.: Serpiginous syphilid and nonsyphilitic aortitis, 221
Scabies in apes, 538
in camels, 538
Norwegian, 499
Scalp, cutis verticis gyrata and acromegaly, *1092
Diseases: See under names of diseases, as Ringworm; Seborrhea; Tinea; etc.
microsporosis caused by Microsporum fulvum; report of case and description of fungus, *610
naevus cerebriformis (cerebelliformis) of, 704
perifolliculitis capitis abscedens et suffodiens; cutis verticis gyrata; hydradenitis suppurativa, 492
turban tumors; report of case with unusual pathologic findings, including both epidermal and dermal nevi, *15
Scars: See Cicatrix
Schamberg's Disease, case for diagnosis, 393
or pigmented purpuric lichenoid dermatitis, 963
Scheer, M.: Parapsoriasis; case for diagnosis, 393
Pyoderma or iododerma, 169
Schamberg's disease; case for diagnosis, 393
Schildkraut, J. M.: Poikiloderma or lupus erythematosus, 748
Schiller, A. E.: Localized amyloidosis of legs, 723
Schistosomiasis, pathology of schistosome dermatitis, *410
Schmidt, F. R.: Action of iodine on diseases of skin as influenced by season and weather, *1083
Adenoma sudoriferum, 203
Liposarcoma, 202
Localized solid edema of extremities (myxedema), 1148
Schmidt, O. E. L.: Erythroplasia of penis, 673
Schoch, A. G.: Mapharsen in treatment of 40 patients following arsphenamine dermatitis, *919
Scholtz, J. R.: Localized scleroderma, 496
Myelogenous leukaemia cutis, 495
Tuberculosis cutis or lupoid sycosis, 494
Schonberg, I. L.: Cheilitis exfoliativa, 370
Dermatitis exfoliativa, 368
Dermatitis herpetiformis, 371
Schools, frequency of certain dermatoses in high school girls; report on 4,700 girls, *475
Schorr, H. C.: Bowen's disease, 513
Lupus pernio; case for diagnosis, 200
Schroeder, T.: "Spiritual" value of syphilis, *470
Schwartz, L.: Occupational leukoderma, *993
Schwartz, W. F.: Primary cutaneous Hodgkin's disease, 500
Schwarzschild, L.: Comparison of old tuberculin (Koch) and modified tuberculin (Mellon and Beinhauer); cutaneous reactions in persons with hyperergic and with anergic tuberculoderms, *461
Sclerema: See Scleroderma
Sclerodactylia: See Scleroderma
Scleroderma, circumscribed, of cheek; case for diagnosis, 1151
diffuse morpheiform type with calcinosis (Thibierge-Weissenbach syndrome); improvement under prostigmine bromide therapy, 740
due possibly to adrenal neoplasm, 969
generalized, 1135
in bands and parathyroidectomy, 486
linear, with facial hemiatrophy, 741
localized, 496
localized; lingua geographica; hypertrichosis; keratosis pilaris, 184
morphea guttata; differential diagnosis, *770
morphea or lichen sclerosus et atrophicus of Hallopeau, 383
over right pectoralis muscle, associated with calcification of right subdeltoid bursa, 688

Scleroderma—Continued
progressive type, 183
sclerema adiposum neonatorum, 487
sclerodactylia, 173
treated with mecholyl iontophoresis, 502
with secondary unilateral muscular atrophy, 385
Sclerosing solutions; photographic method for studying their effects on tissue, *86
Sclerosis, tertiary syphilis; gumma of soft palate, interstitial sclerosis of testicle, asymptomatic cerebrospinal syphilis and aortitis, 373
tuberous, and adenoma sebaceum, 1150
Scrofula: See Tuberculosis
Scrofuloderma: See Tuberculids; Tuberculosis
Scrotum, nodular circumscribed giant lichenification of, 145
Seasons, action of iodine on diseases of skin as influenced by season and weather, *1083
Sebaceous Glands, adenoma sebaceum and tuberous sclerosis, 1150
Seborrhea, seborrheic dermatitis in cow and calf, 535
seborrheic dermatitis, parapsoriasis or cutaneous manifestation of endocrine dysfunction, 731
seborrheic eczema, familial; case for diagnosis, 355
use of vitamin P-P in treatment of seborrhea and acne; preliminary note, 145
Secretions, Internal: See Endocrine Glands
Section on Dermatology and Syphilology of American Medical Association, program notice, 658
Sedormid: See Ureides
Seidowitz, M.: Treatment of dermatophytosis pedis with medicated insoles, *576
Senear, F. E.: Arsenical keratoses, 191
Dermatitis herpetiformis in child; case for diagnosis, 198
Lupus pernio; case for diagnosis, 200
Macular atrophy; case for diagnosis, 193
Macular atrophy (Schwenninger and Buzzi type), 194
Mycosis fungoides; case for diagnosis, 510
Mycosis fungoides (prefungoid stage), 510
Myelogenous leukemia, 195
Senear-Usher Syndrome: See Pemphigus
Senility: See Old Age
Shaffer, B.: "Open bite" in association with prenatal syphilis, 733
Pemphigoid eruption associated with hemorrhagic nephritis following bismuth therapy; report of case, *59
Psoriasis associated with lichen-spinulosus-like eruption, 734
Shaffer, L. W.: Lupus erythematosus; case for diagnosis, 712
Sharlit, H.: Herpes progenitalis as venereal contagion, *933
Reticuloendotheliosis; mycosis fungoides (?), 699
Shaw, C.: Neurosyphilis and late syphilis of skin, mucous membranes and bones, *456
Sheep Pox, human infection with ecthyma contagiosum, virus disorder of sheep; report of 2 cases, *878
Shellow, H.: Discoloration of nails due to nail enamel, *480
Shelmire, B.: Nature of excitant of poison ivy dermatitis, *405
Shelton, J. M.: Fistula from retained dental root, *938
Shepard, J. H.: Pseudoxanthoma elasticum, 680
Shoes, treatment of dermatophytosis pedis with medicated insoles, *576
Short Waves: See under names of organs and regions
Shoulder, fibrosarcoma of; case for diagnosis, 195
Shwartzman Phenomenon: See Immunity
Silkworms, contact reactions in atopy; contact reactions to silkworm in atopic subjects, 949
Silver, H.: Atrophy of subcutaneous fat due to protamine zinc insulin, 986
Early syphilitic macular atrophy, 983
Sarcoidosis, 522
Silver: See also Stains and Staining
toxicity; argyria, 493, 1147
Silvers, S. H.: Darier's disease (keratosis follicularis), 1172
Pseudoxanthoma elasticum with angioid streaks of retina, 155, 1167
Xanthoma diabeticorum, 1169
Skeer, J.: Diffuse pigmentation; incontinentia pigmentii, 148
Ehlers-Danlos syndrome, *450
Erythema multiforme; case for diagnosis, 1164
Hypertrophic scarring following eczema vaccinatum, 1165
Skeleton: See Bones
Skin and Cancer Unit of New York Post-Graduate Medical School and Hospital, Columbia University; historical review, *112
Skin: See also Dermatology
Abnormalities: See also Atrophy; Pigmentation; etc.
abnormalities; congenital cutaneous defects caused by form of epidermolysis bullosa, 487
abnormalities; dermatolysis; case for diagnosis, 384
abnormalities; Ehlers-Danlos syndrome, *450, 742
abnormalities; senile elastosis; acrodermatitis chronica atrophicans, 1167
Atrophy: See Atrophy
Cancer: See Cancer; Epithelioma; Sarcoma; etc.
chemistry; histochemical study of neurodermatitis; preliminary report; microincineration and spectrographic analysis, *109
Diseases: See also Dermatitis; and under names of diseases, as Eczema; Herpes; Mycosis, cutaneous; etc.; and under names of plants and drugs, as Arsphenamines; Rhus; etc.
diseases; action of iodine on diseases of skin as influenced by season and weather, *1083
diseases, and environment, 1129
diseases; dermatology and folklore, 1129
diseases; flesh-colored paste to camouflage cutaneous lesions, 224
diseases; frequency of certain dermatoses in high school girls; report on 4,700 girls, *475
diseases; local conditions favoring cutaneous diseases, 349
diseases; presentation of cases of cutaneous diseases in animals, 532
diseases; proposed classification of cutaneous lipoidoses with description of new local lipoid dermatosis: imbibitio lipoidica collageni degenerati cutis, *68
diseases; pyogenic infections in dogs, 537
diseases; symposium on allergic dermatoses; allergic occupational dermatosis, 1128
diseases; symposium on cutaneous diseases in animals; dermatoses of wild animals in captivity, 538
diseases; symposium on cutaneous diseases in animals; introduction, 530
diseases; symposium on cutaneous diseases in animals; roentgen rays in treatment of diseases in animals, 533
diseases; symposium on cutaneous diseases in animals; some common cutaneous diseases in domesticated animals with correlation of same diseases in man, 535
diseases; use of colloidal calomel (mild mercurous chloride) ointment in dermatology, 345
diseases; use of sulfanilamide in dermatology, *33

Skin—Continued
diseases; use of sulfanilamide in streptococcic dermatoses, 144
effect of ointment bases on skin; results of patch tests with commonly used ointment bases, *285
effect of ultraviolet radiation on roentgen rays; do ultraviolet rays have deleterious effect on roentgen rays when applied to skin? *466
experiments on histamine as chemical mediator for cutaneous pain, 949
Gangrene: See Gangrene
Hemorrhage: See Purpura
Inflammation: See Dermatitis
personality factor in psychoneurogenous reactions of skin, *780
Pigmentation: See under Pigmentation
psychoneurogenous component of cutaneous reaction mechanisms, 947
Syphilis: See Syphilids
Tuberculosis: See Tuberculids; Tuberculosis
Tumors: See under Tumors
Ulcers: See Ulcers
Slepyan, A. H.: Parapsoriasis; case for diagnosis, 1145
Slone, J.: Acetylglycarsenobenzene in treatment of syphilis; preliminary report, *1046
Slush Method: See under Acne
Smallpox, amount and duration of immunity induced by intradermal inoculation of cultured vaccine virus, 949
hypertrophic scarring following eczema vaccinatum, 1165
Snails: See Schistosomiasis
Snell, F. D.: Gentian violet in Sabouraud's medium for isolation of pathogenic fungi, *308
Sniderman, H. R.: Late syphilis with rare orbital gumma; report of case, *559
Sobel, N.: Symposium on syphilis; acute hemorrhagic encephalitis due to neoarsphenamine, with recovery, 665
Symposium on syphilis; lichen-planus-like recurrent syphiloderm with severe itching, 670
Sobisminol: See Syphilis
Sobotka, H.: Massive arsenotherapy in early syphilis by intravenous drip method; arsenic excretion in urine and concentration in blood, *270
Societies, American Academy of Dermatology and Syphilology; annual meeting, 946
American Board of Dermatology and Syphilology; examination for certification, 343
dermatologic, directory of, 235, 751
foreign, directory of, 235, 751
international, directory of, 235, 751
local, directory of, 237, 753
national, directory of, 235, 751
Pacific Northwest Dermatological Society, 658
sectional, directory of, 236, 752
state, directory of, 236, 752

Society Transactions:
Atlantic Dermatologic Conference, 685
Baltimore-Washington Dermatological Society, 350
Bronx Dermatological Society, 214, 522, 982
Brooklyn Dermatological Society, 148
Chicago and Detroit Dermatological Societies, 705
Chicago Dermatological Society, 185, 508, 1131
Cleveland Dermatological Society, 367, 673
Los Angeles Dermatological Society, 356, 488
Manhattan Dermatologic Society, 159, 389, 968
Minnesota Dermatological Society, 395
New York Academy of Medicine, Section of Dermatology and Syphilis, 174, 374, 665, 953, 1162
New York Dermatological Society, 203, 726, 1151
Philadelphia Dermatological Society, 224, 530, 733

Sodium Bismuthate: See under Syphilis
Gold Thiosulfate: See Gold and Gold Compounds
morrhuate, toxic eruption following injections of, 1149
Salicylate: See under Salicyl Compounds
Spectrography: See Skin, chemistry
Spiegel, L.: Symposium on syphilis; arsenical dermatitis; monorecidive, followed by arsenical dermatitis; syphilitic onychia due to arsenic? 671
Symposium on syphilis; bilateral paralysis of abducens nerve following lumbar puncture, 667
Spinal Fluid: See Cerebrospinal Fluid
Spinal Puncture, symposium on syphilis; bilateral paralysis of abducens nerve following lumbar puncture, 667
Spirochaeta microdentium; massive destruction of face, *1040
Pallida: See Syphilis
Splenomegaly, sarcoid type of tuberculosis in American Negro, with splenomegaly, 747
Stains and Staining, granuloma inguinale, 1124
Staphylococci, staphylococcic dermatitis in Irish setter, 532
staphylococcic impetigo contagiosa, *840
Starch: See under Lupus vulgaris
Stenhouse, E. E.: Atrophia pilorum, 1133
Stewart, C. D.: Dermatitis due to mesquite wood; report of case, *937
Stillians, A. W.: Pemphigus limited to mucosa and conjunctiva, 186
Stokes, J: Herxheimer reaction, gumma or nonspecific infected granuloma, 736
Stokes, J. H.: Personality factor in psychoneurogenous reactions of skin, *780
Stomatitis and gold dermatitis, 721
Stools: See Feces
Stout, O. M.: Keloid and depressed scars subsequent to ecthymatous rupioid syphilids, 503
Lichen planus of lips and mouth, 505
Norwegian scabies, 499
Parenteral use of hypertonic dextrose for relief of pruritus and of serum sickness, *802
Perifolliculitis capitis abscedens et suffodiens; cutis verticis gyrata; hydradenitis suppurativa, 492
Streptococci: See also Erysipelas
cellulitis of elephantiasis nostras type (recurrent), 738
epidermolysis bullosa; clinical and bacteriologic study; report of 4 cases, *884
infection of ears, 738
use of sulfanilamide in streptococcic dermatoses, 144
Stryker, G. V.: Pyoderma chancriforme faciei, *447
Stuyvesant Square Hospital, Skin and Cancer Unit of New York Post-Graduate Medical School and Hospital, Columbia University; historical review, *112
Sucrets: See under Resorcinol and Resorcinol Derivatives
Sudoriparous Glands: See under Sweat Glands
Sulfanilamide and Sulfanilamide Derivatives, sulfapyridine dermatitis; report of 2 cases, *341
Therapy: See Chancroid; Dermatitis herpetiformis; Erysipelas; Leishmaniasis; Skin, diseases; Streptococci; Ulcers; etc.
use of sulfanilamide in dermatology, *33
Sulfapyridine: See Dermatitis herpetiformis; Sulfanilamide and Sulfanilamide Derivatives
Sulzberger, M. B.: Chronic discoid and lichenoid exudative dermatosis, 220
Eczema venenatum due to wooden bracelet, 216
Eczema venenatum (dye in clothing), 988
Eczema venenatum from nail polish, 218
Fungating iodide eruption of tongue or squamous cell epithelioma of tongue, 528

Sulzberger, M. B.—Continued
Melanodermatitis, 990
Squamous cell epithelioma of tongue or fungating iodide eruption of tongue, 990
Sunburn: See Light, toxicity
Sunlight: See under Light
Swartz, J. H.: Extensive lichenified eruption caused by Trichophyton rubrum, *614
Sweat Glands, adenoma sudoriferum, 203
hidradenitis suppurativa, 1142
perifolliculitis capitis abscedens et suffodiens; cutis verticis gyrata; hydradenitis suppurativa, 492
studies on secretion of sweat in newborn, 663
syringocystoma confined to face, 510
Sweitzer, S. E.: Xanthoma tuberosum and myxedema; report of case, *419
Sycosis, lupoid, or tuberculosis cutis, 494
Syphilids, keloid and depressed scars subsequent to ecthymatous rupioid syphilids, 503
or psoriasis, 978
palmar, psoriasis or eczema, 502
serpiginous, and nonsyphilitic aortitis, 221
Syphilis: See also Chancre; Syphilids; Venereal Diseases; and under names of organs and regions, as Cardiovascular System; Elbow; Hand; etc.
acetylglycarsenobenzene in treatment; preliminary report, *1046
acute interstitial myocarditis following administration of arsphenamines, *312
arsenoresistant, 358
arsphenamine encephalopathy; report of unusual clinical and histologic observations, *814
chronic ulcer of back; tumor of leg (syphilis or dermatitis artefacta?), 691
congenital, trisodium arsphenamine sulfonate (trisodarsen) in treatment, 483
early syphilitic lesions mistaken for dermatophytosis, *11
early syphilitic macular atrophy, 983
early syphilitic osteomyelitis with report of 2 cases, 483
effect produced on newly contracted syphilis by transfusion of blood taken from patients affected with late stages of syphilis, 1125
effects of neoarsphenamine and mapharsen on formed elements of blood; granulocytopenia following neoarsphenamine therapy in patient who subsequently received mapharsen without untoward reaction, *909
excretion of bismuth in urine of patients treated with bismuth ethylcamphorate, *1073
Herxheimer reaction, gumma or nonspecific infected granuloma, 736
infectious relapse of more than 2 years' duration, 142
iodobismitol with saligenin in treatment of neurosyphilis, *46
juxta-articular nodes, 515
lag in reversal of blood serologic tests under bismuth in course of combined chemotherapy, 483
late syphilis with rare orbital gumma; report of case, *559
mapharsen in treatment in office practice; study based on 2,342 injections of 113 patients, 345
mapharsen in treatment of 40 patients following arsphenamine dermatitis, *919
massive arsenotherapy in early syphilis by continuous intravenous drip method; arsenic excretion in urine and concentration in blood, *270
massive arsenotherapy in early syphilis by continuous intravenous drip method; clinical considerations, *253
massive arsenotherapy in early syphilis by continuous intravenous drip method; follow-up observations at Bellevue Hospital, *267
massive arsenotherapy in early syphilis by continuous intravenous drip method; follow-up observations at New York Hospital, *264
Syphilis—Continued
massive arsenotherapy in early syphilis by continuous intravenous drop method; preliminary work with neoarsphenamine, *239
massive arsenotherapy in early syphilis by continuous intravenous drip method; public health aspects, *283
massive arsenotherapy in early syphilis by continuous intravenous drip method; résumé of serologic observations, *262
massive arsenotherapy in early syphilis by continuous intravenous drip method; technic, *245
massive arsenotherapy in early syphilis by continuous intravenous drip method; toxicologic manifestations, *248
massive dose arsenotherapy by intravenous drip method, 1124
massive dose chemotherapy of early syphilis by intravenous drip method, 142
menstrual cycle and blood serologic test for, 484
mobilization of bismuth produced by ammonium chloride, *868
moist papules in axilla, *656
neurosyphilis and late syphilis of skin, mucous membranes and bones, *456
nonspecific effect of antisyphilitic treatment in inflammatory ocular lesions (chorioretinitis), 225
of hand; neurodermatitis of calf, 965
"open bite" in association with prenatal syphilis, 733
prognosis with reference to late complications in cardiovascular system, 951
quartan malaria in treatment of neurosyphilis, 1124
reexamination of cases of fresh syphilis treated in 1912-1913 (preliminary report), 951
review of recent literature, 948
serologic discrepancies in, 344
sobismuinol mass; clinical results with oral administration, 346
"spiritual" value of, *470
study to evaluate original serologic tests for syphilis, 343
symposium on; acute hemorrhagic encephalitis due to neoarsphenamine, with recovery, 665
symposium on; arsenical dermatitis; monorecidive, followed by arsenical dermatitis; syphilitic onychia due to arsenic? 671
symposium on; bilateral paralysis of abducens nerve following lumbar puncture, 667
symposium on; lichen-planus-like recurrent syphiloderm with severe itching, 670
syphilitic chancre acquired by newborn infant during delivery, 661
syphilitic dactylitis; case for diagnosis, 680
syphilitic glossitis, 521
tertiary; gumma, Herxheimer reaction or nonspecific infected granuloma, 736
tertiary; gumma of soft palate, interstitial sclerosis of testicle, asymptomatic cerebrospinal syphilis and aortitis, 373
tertiary (gummas of arm), 682
tertiary, livedo racemosa type of, 973
tertiary, or tuberculosis of elbow joint, 683
tertiary, tuberculosis or both, 711
treated, prognosis of, 951
trophic elbow joint due to syringomyelia or tertiary syphilis with Charcot joint, 682
tuberculosis of lungs in patients with sarcoidosis, granuloma annulare and lupus erythematosus; comparison, based on roentgenologic statistics, with its incidence in patients with proved tuberculosis of skin and with different stages of syphilis, *1
unusual serologic reactions during pregnancy, *137
vaginal melanosis caused by bismuth therapy and carcinoma of cervix, *23
Wassermann test; effect of antisyphilitic drugs on Wassermann reaction, 484

Syphiloderm: See Syphilis
Syphiloid of cat, 536
Syringocystoma confined to face, 510
Syringomyelia, trophic elbow joint due to syringomyelia or tertiary syphilis with Charcot joint, 682

Tabes Dorsalis, Charcot's disease of ankle, 171
immunologic investigations, particularly of lysin, in spinal fluid of tabetic patients infected with relapsing fever, 664
pathology and pathogenesis of syphilitic primary optic atrophy, 484
Tar: See also under Lymphoblastoma
dermatophytosis resembling contact dermatitis (cement and tar), 361
Teeth, dachshund with carcinoma at site of incisor tooth; treatment by roentgen rays, 533
fistula from retained dental root, *938
injuries of mouth caused by teeth, *333
"open bite" in association with prenatal syphilis, 733
Telangiectasia: See also Angioma; Purpura annularis telangiectodes
following infantile eczema, 506
telangiectatic dysplasia of Rendu-Osler-Weber type, with pigmentary changes, 231
telangiectatic nevus, 977
with atrophoderma, 187
Templeton, H. J.: Cheilitis and dermatitis from resorcinol and derivative (sucrets), *138
Testicles, tertiary syphilis; gumma of soft palate, interstitial sclerosis of testicle, asymptomatic cerebrospinal syphilis and aortitis, 373
Theelin: See Estrogens
Thiamine Chloride: See Vitamins, B
Thibierge-Weissenbach Syndrome: See Calcification
Thiosulfates, effect on arsenic excretion, *399
Thomas, C. C.: Diffuse morpheiform type of scleroderma with calcinosis (Thibierge-Weissenbach syndrome); improvement under prostigmine bromide therapy, 740
Sarcoid type of tuberculosis in American Negro, with splenomegaly, 747
Thomas, E. W.: Early syphilitic lesions mistaken for dermatophytosis, *11
Massive arsenotherapy in early syphilis by continuous intravenous drip method; follow-up observations at Bellevue Hospital, *267
Relapsing early acute arsenical erythema; report of 2 cases, *30
Thrombocytopenia: See Purpura haemorrhagica
Thurmon, F. M.: Excretion of bismuth in urine of patients treated with bismuth ethylcamphorate, *1073
Thyroid: See Myxedema
Ticks: See also Relapsing Fever
wood ticks; easy method for removal from skin, *937
Tinea: See also Ringworm
Amiantacea: See Seborrhea
circinata; fungous infections, 538
corporis; dermatophytosis, 962
Decalvans: See Alopecia areata
Imbricata: See Ringworm
Tissue, sclerosing solutions; photographic method for studying their effects on tissue, *86
Tobin, W. W.: Case for diagnosis, 519
Dermatofibrosarcoma protuberans, 1140
Epidermolysis bullosa acquisita, 517
Erythema figuratum perstans, 1143
Lupus vulgaris, 201
Pityriasis rubra pilaris, 513
Psoriasis with pustular exacerbation, 1136
Tuberculosis verrucosa cutis, 1141
Toe-Nails: See Nails
Toes: See Fingers and Toes
Tongue, black hairy tongue; report of 3 cases, *566
chronic ulceration of; case for diagnosis, 979
Tongue—Continued
fungating iodide eruption of tongue or squamous cell epithelioma of tongue, 528, 990
localized amyloidosis of tongue, pharynx and eyelids, 723
localized scleroderma; lingua geographica; hypertrichosis; keratosis pilaris, 184
lupus erythematosus involving tongue, 497
nonspecific granuloma on dorsum of tongue of dog; treatment by roentgen rays, 534
pigmentation due to bismuth, 223
squamous cell epithelioma of, 985
syphilitic glossitis, 521
Torula, torulosis involving human cerebrum, 140
Toxicodermas: See Dermatitis, venenata; Drugs, eruptions
Traenkle, H. L.: Epithelioma adenoides cysticum, trichoepithelioma and basal cell cancer; relation between these diseases, as shown by histologic studies of multiple benign cystic epithelioma, *822; correction, 1174
Traub, E. F.: Cheilitis, 1161
Eczema simulating lymphoblastoma (mycosis fungoides), 203
Extensive lupus vulgaris treated by surgical methods, 1152
Leukemia and leukemid, 214
Leukemia of skin, 1162
Leukemid; case for diagnosis, 1156
Lymphatic leukemia, 687
Necrobiosis lipoidica diabeticorum without diabetes, 693
Pemphigus; case for diagnosis, 700
Trauma: See under Mouth; etc.
Treponematosis: See Frambesia; Syphilis
Trichoepithelioma, epithelioma adenoides cysticum and basal cell cancer; relation between these diseases, as shown by histologic studies of multiple benign cystic epithelioma, *822; correction, 1174
Trichophytid: See Trichophytosis
Trichophytin: See Trichophytosis
Trichophyton, fungistatic power of blood serum, *426
Trichophytosis: See also Mycosis
extensive lichenified eruption caused by Trichophyton rubrum, *614
Trichotillomania: See under Hair
Trisodarsen: See Syphilis
Tryparsamide, sensitization to arsenical compounds; sensitization to pentavalent arsenical following use of trivalent arsenical, *808
Tubercle Bacilli: See also Tuberculosis
lupus erythematosus due to, 145
Tuberculids: See also under Tuberculosis
micropapular, *625
papulonecrotic, 675
papulonecrotic, or granuloma annulare, 386
papulonecrotic, or lupus erythematosus, 374
rosacea-like, 496
with rosacea-like manifestations, 387
Tuberculin: See under Tuberculosis
Tuberculosis: See also under Elbow; Lymph Nodes; Mucous Membrane
comparison of old tuberculin (Koch) and modified tuberculin (Mellon and Beinhauer); cutaneous reactions in persons with hyperergic and with anergic tuberculoderma, *461
cutaneous reactivity of guinea pigs to gum arabic (acacia), 950
cutis or lupoid sycosis, 494
noncaseating, of skin, 708
of skin, 158, 523
or tertiary syphilis of elbow joint, 683
primary, of skin, 705
primary tuberculous infection of skin, 664
primary tuberculous infection of skin and mucous membrane, 147
pulmonary; lupus vulgaris disseminatus; roentgen ray dermatitis, 1171

Tuberculosis—Continued
pulmonary; results of pulmonary roentgenologic studies of patients with lupus erythematosus, 348
pulmonary; tuberculosis of lungs in patients with sarcoidosis, granuloma annulare and lupus erythematosus; comparison, based on roentgenologic statistics, with its incidence in patients with proved tuberculosis of skin and with different stages of syphilis, *1
sarcoid type in American Negro, with splenomegaly, 747
tertiary syphilis or both, 711
tuberculin reactions in lupus erythematosus, 348
verrucosa cutis, 1141
verrucosa cutis of more than 60 years' duration, 676
Tulipan, L.: Epidermolysis bullosa acquisita, 175
Kaposi's sarcoma, 174
Tumors: See also Adenoma; Angioma; Cancer; Epithelioma; Hemangioma; Lymphangioma; Lymphocytoma; Melanoma; Papilloma; etc.; and under names of organs and regions, as Adrenals; Eyelids; Legs; Pituitary Body; etc.
dermoid, of eye in dachshund, 532
Ehlers-Danlos syndrome, *450
glomus tumor; doubts and difficulties in diagnosis, 143
turban tumors; report of case with unusual pathologic findings, including both epidermal and dermal nevi, *15
Twining, H. E.: Keratosis palmaris et plantaris, acquired type, or Haxthausen's disease, 232
Reticuloendotheliosis, 748
Twins, Parrot's pseudoparalysis in pair of twins of same sex, 950
Recklinghausen's disease in identical twins, *657

Ulcers: See also under names of organs and regions, as Anus; Back; Legs; Lips; Nose; Tongue; etc.
multiple recurrent disseminated painful ulcers; case for diagnosis, 696
ulcerative reaction from gentian violet in treatment of impetigo contagiosa, *1122
Varicose: See Varicose Veins
Ultrashort Waves: See under names of organs, regions and diseases
Ultraviolet Rays: See also Light
effect of ultraviolet radiation on roentgen rays; do ultraviolet rays have deleterious effect on roentgen rays when applied to skin? *466
Therapy: See under names of organs, regions and diseases
Umansky, M.: Early Raynaud's syndrome; case for diagnosis, 222
Erythrose peribuccale pigmentaire (Brocq), 989
Universities, clinical study of acne in university students, 344
Urbach, E.: Proposed classification of cutaneous lipoidoses with description of new local lipoid dermatosis: imbibitio lipoidica collageni degenerati cutis, *68
Ureides, purpura haemorrhagica resulting from sedormid, 141
Ureters, arsenic as cause of cancer of mucous membrane; report of case, *641
Urine, effect of thiosulfate on arsenic excretion, *399
excretion of bismuth in patients treated with bismuth ethylcamphorate, *1073
massive arsenotherapy in early syphilis by intravenous drip method; arsenic excretion in urine and concentration in blood, *270
Urticaria pigmentosa (adult type), 967
pigmentosa (bullous type), 975
Usher-Senear Syndrome: See Pemphigus

Uterus, vaginal melanosis caused by bismuth therapy and carcinoma of cervix, *23
Uvea, inflammation; sarcoid of Boeck with uveitis and keratitis, 489
Uveitis: See Uvea, inflammation

Vaccines: See under Nails
Vaccinia: See Smallpox
Vagina, vaginal melanosis caused by bismuth therapy and carcinoma of cervix, *23
Varicose Veins, sclerosing solutions; photographic method for studying their effects on tissue, *86
toxic eruption following injections of sodium morrhuate, 1149
Varix: See Varicose Veins
Veins: See Blood vessels; Cardiovascular System; Embolism
Varicose: See Varicose Veins
Venereal Diseases: See also Chancre; Chancroid; Syphilis
herpes progenitalis as venereal contagion, *933
Vero, F.: Dermatitis medicamentosa (mapharsen), 967
Papulonecrotic tuberculid or lupus erythematosus, 374
Schamberg's disease or pigmented purpuric lichenoid dermatitis, 963
Verruca, digitate, on inside of ear of dog; treatment by roentgen rays, 534
multiple, in mouth and on gums of dog; treatment by roentgen rays, 534
plantaris, *302
superficial noninflammatory lesions of feet, 234
Tuberculous: See under Tuberculosis
verrucous nevus of groin, hands and feet; case for diagnosis, 356
Vesication, vesicant chemical warfare agents, *123
Veterinary Medicine, presentation of cases of cutaneous diseases in animals, 532
symposium on cutaneous diseases in animals; dermatoses of wild animals in captivity, 538
symposium on cutaneous diseases in animals; introduction, 530
symposium on cutaneous diseases in animals; parasites affecting skin, 535
symposium on cutaneous diseases in animals; roentgen rays in treatment of diseases in animals, 533
Virilism, acanthosis nigricans asociated with masculinizing syndrome, 493
Viruses: See also Herpes; etc.
human infection with ecthyma contagiosum, virus disorder of sheep; report of 2 cases, *878
Vitamins: See also Pellagra; etc.
A; lichen planus followed by lichen pilaris (vitamin A deficiency?), 165
avitaminosis, 193
B; acrodynia treated with intramuscular injections of vitamin B_1, 486
B; antiacrodynic properties of certain foods, 659
B deficiency, 720
evaluations of vitamins A, B_1 and C as therapeutic agents, 661
P-P: See Acne; Seborrhea
treatment of occupational dermatitis with vitamins A and D, 146
vitamin (A and B) deficiency, 720
Vitiligo, 676
leukoderma acquisitum centrifugum, 351, 720
occupational leukoderma, *993
occupational leukoderma; preliminary report, 141
Vulva, anogenital ulcerations on embolic base, 951
chronic chancroid of vulva, perineum and inguinal regions, 369
epidermoid carcinoma in Shetland pony; treatment by roentgen rays, 534
Esthiomene: See Lymphogranuloma Venereum
kraurosis vulvae; differential diagnosis, *775

Walzer, A.: Alopecia cicatrisata (pseudopelade of Brocq), 1170
Erythema elevatum diutinum; case for diagnosis, 154
Erythema figuratum (erythema annulare centrifugum of Darier?), 1172
Indolent ulceration of leg, 152
Mycosis fungoides; case for diagnosis, 1162
Pityriasis rubra pilaris, 153
Senile elastosis; acrodermatitis chronica atrophicans, 1167
War, vesicant chemical warfare agents, *123
Warren, L. H.: Occupational leukoderma, *993
Warts: See Verruca
Wassermann Reaction: See also Syphilis
effect of antisyphilitic drugs on, 484
Weather, action of iodine on diseases of skin as influenced by season and weather, *1083
Weber, L. F.: Syringocystoma confined to face, 510
Toxic eruption following injections of sodium morrhuate, 1149
Weber-Christian's Disease: See Panniculitis
Weber-Rendu-Osler's Disease: See Telangiectasia
Webster, B.: Massive arsenotherapy in early syphilis by continuous intravenous drip method; follow-up observations at New York Hospital, *264
Weidman, F. D.: Symposium on cutaneous diseases in animals; dermatoses of wild animals in captivity, 538
Weise, E. C.: Naevus cerebriformis (cerebelliformis) of scalp, 704
Weissenbach-Thiblerge Syndrome: See Calcification
Welsh, A. L.: Use of drill on diseased nails, *1123
Welton, D. G.: Keratosis follicularis, 354
Wheal: See Urticaria
Wieder, L. M.: Cutis verticis gyrata and acromegaly, *1092
Wien, M. S.: Hidradenitis suppurativa, 1142
Wiener, K.: Vaginal melanosis caused by bismuth therapy and carcinoma of cervix, *23
Wile, U. J.: Acute disseminated lupus erythematosus; its treatment with sulfanilamide and allied products, *1059
Early mycosis fungoides, 718
Erythema figuratum perstans; case for diagnosis, 724
Generalized herpes zoster associated with leukemia, *587
Gold dermatitis and stomatitis, 721
Leukoderma acquisitum centrifugum, 720
Localized amyloidosis of legs, 723
Localized amyloidosis of tongue, pharynx and eyelids, 723
Lupus miliaris disseminatus faciei or lichen planus, 710
Lupus vulgaris, 707
Lupus vulgaris of cheek, 706
Lupus vulgaris of nose, 707
Multiple pigmented nevi, 720
Necrobiosis without diabetes, 719
Wile, U. J.—Continued
Noncaseating tuberculosis of skin, 708
Pemphigus erythematodes (Senear-Usher syndrome), 713
Pemphigus vulgaris, 715
Pityriasis-rosea-like dermatitis following gold therapy; report of 2 cases, *1105
Primary tuberculosis of skin, 705
Sarcoid, 708
Tuberculosis, tertiary syphilis or both, 711
Vitamin (A and B) deficiency, 720
Vitamin B deficiency, 720
Wilhelm, L. F. X.: Arsenic as cause of cancer of mucous membrane; report of case, *641
Williams, T. L.: Mobilization of bismuth produced by ammonium chloride, *868
Wilson, D. J.: Wood ticks; easy method for removal from skin, *937
Winer, L. H.: Pseudoepitheliomatous hyperplasia, *856
Xanthoma tuberosum and myxedema; report of case, *419
Wirtschafter, Z. T.: Transverse furrows of nails, *874
Wise, F.: Acanthosis nigricans; case for diagnosis, 1159
Circumscribed scleroderma of cheek; case for diagnosis, 1151
Leprosy with juxta-articular nodes, 1162
Mycosis fungoides, leukemid or Hodgkin's disease of skin, 1157
Wolff, M. J.: Lipoidosis or necrobiosis lipoidica diabeticorum, 363
Wood, dermatitis due to mesquite wood; report of case, *937
eczema venenatum due to wooden bracelet, 216
Workmen's Compensation and Insurance: See Industrial Diseases
Wright, C. S.: Dermatitis herpetiformis or "id," 230

Xanthelasma: See Xanthoma
Xanthoma, angina pectoris in hereditary xanthomatosis, 948
diabeticorum, 1169
juvenile, 395
tuberosum, 367
tuberosum and myxedema; report of case, *419
tuberosum multiplex, 152
xanthelasma associated with leprosy, 972
xanthomatosis, 512
Xanthomatosis: See Xanthoma
Xeroderma pigmentosum in Negress, *570

Yaws: See Frambesia
Yeast: See also Fungi
effect of dyes on yeast fungi, 349

Zakon, S. J.: Juxta-articular nodes; syphilis, 515
Kaposi's sarcoma, 192
Zeisler, E. P.: Cutis verticis gyrata and acromegaly, *1092
Zona: See Herpes zoster